Access to human genetic resources: materials from a transnational stakeholder dialogue

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Materials from a Transnational Stakeholder Dialogue

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SUMMARY STATEMENT

This report summarizes deliberations over the *Access to Human Genetic Resources* held during a stakeholder dialogue process launched by the World Business Council for Sustainable Development (WBCSD) in 2001/2002. The dialogue process was designed to explore options of companies to address contested issues of intellectual property in their business strategies. To that end, companies were exposed to the concerns of stakeholders and urged to define responses to these concerns. The project involved major companies and transnational non-governmental organizations as well as renowned experts in the field of intellectual property rights.

This paper briefly sketches the project and the process of the dialogue. The products of the process are the opinions, both concurring and dissenting, that the participants reached on the access to human genetic resources, subsumed in the final report to the WBCSD that emerged from the project. This paper also reviews documents (Circulars) from the proceedings, which further illustrate the dynamics of the deliberations, and the range and direction of arguments exchanged by the participants.

ZUSAMMENFASSUNG

Das Diskussionspapier stellt die Ergebnisse dar, die im Rahmen eines vom World Business Council on Sustainable Development (WBCSD) initiierten Stakeholder Dialogs zum Thema Zugang zur humangenetischen Ressourcen erreicht worden sind. Ziel des Dialogs war es zu untersuchen, welche Optionen Unternehmen haben, öffentlichen Kritiken am geltenden Regime des geistigen Eigentums durch Anpassung ihrer Strategien Rechnung zu tragen. Beteiligt waren an dem Dialog Vertreter von großen pharmazeutischen Firmen und von transnational operierenden Nichtregierungsorganisationen, sowie Experten des Rechts des geistigen Eigentums.

Das Diskussionspapier skizziert Charakter und Verlauf des Dialogverfahrens. Im Zentrum stehen die Ergebnisse zum Thema Zugang zur humangenetischen Ressourcen, wie sie in den vom World Business Council herausgegebenen Endberichts des Stakeholder Dialogs eingegangen sind — mit der Kennzeichnung der jeweils übereinstimmenden oder abweichenden Positionen der Teilnehmer. Es folgt eine kurze Diskussion dieser Ergebnisse. Im Anhang werden zentrale Dokumente des Verfahrens (Circulars) abgedruckt, die Einblick geben in die Dynamik der Verhandlungen und die Reichweite und Richtung der von den Teilnehmern ausgetauschten Argumente.

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1. The Project: In Search of New IPR Policy Options for Pharmaceutical Companies

In 2001 the World Business Council for Sustainable Development (WBCSD) launched a project to engage transnational pharmaceutical companies and non-governmental organizations in a dialogue over the proper role and limits of intellectual property rights (IPRs) in the development of medical biotechnology. Project Working Groups dealt with three issues areas that raise broad public concerns and confront companies with the need to reconsider their IPR policies: Access to Human Genetic Resources, Protection of Traditional Knowledge, and Access to Essential Medicines.

The WBCSD is a coalition of 160 international companies sharing a commitment to sustainable development. Council members considered the dialogue project as part of their broader efforts to find options for business strategies that meet the requirements of social, political, and ethical "sustainability". Accordingly, the focus of the project was on what the companies themselves might contribute in order to resolve contested IPR issues, given the economic criteria under which they operate. Participants, of course, had to be aware of existing legal regimes of IPR (in particular, the Agreement on Trade-Related Aspects of Intellectual Property Rights, "TRIPS"), but they were expected to explore options for societal self-regulation within and beyond those regimes.

Some of the rationales and premises underlying the project are described in the following excerpts from the document that outlined the project and called for the participation of the stakeholders[1]:

> **Conflicts over IPRs**
>
> Existing regimes of IPRs are contested. Companies would defend them as a suitable and, in fact, necessary strategy to secure a return on the investments necessary to produce useful knowledge. … Companies hold that these regimes serve a social and not merely a private function: By providing incentives for innovation and mobilizing resources for research IPRs will accelerate and multiply technological development that benefits the whole society. In contrast, critics argue that IPRs, particularly patent protection, in fact create unfair monopolistic advantage and concentrated market control; they defend excessive prices and profits, and deprive societies of the benefits of rapid dissemination and use of new knowledge. … Strong IPRs are suspected of concentrating strategic knowledge in the hands of some exclusive global business players, making it even more difficult for developing countries to gain access to and derive benefits from new technologies. This further exacerbates already existing imbalances in the world economy.

1 Framework for a Stakeholder Dialogue Proposed by the World Business Council for Sustainable Development (WBCSD), downloadable from the internet at: **<http://www.wz-berlin.de/ipr-dialogue>.**

Emerging Patterns of Global Governance

> While the contested issues may ultimately require national or international regulation, regulatory policies may be slow. … Strategies that involve non-state actors (including the business sector) in processes of negotiated policy making and private-public partnerships are likely to coexist with legal international regimes in the emerging processes of global governance. Such strategies give political mandate (and corresponding duties) to global players from the private sector of business and from the civil society sector of non-governmental organizations. This implies that business enterprises are able and willing to address criteria beyond short-term profit making and shareholder value in their corporate policies, and that non-governmental organizations are able and willing to engage in limited taskforce like cooperation in addition to and beyond strategies of protest designed to raise public awareness or encourage public resistance.

The Notion of "Embedded" Economy

> The WBCSD project assumes as given the premise that companies operate on markets that are … to a certain extent at least, also communities where people act as citizens and as stakeholders pursuing social, political, or cultural concerns beyond purely economic interests. … The WBCSD is aware of the social and political embeddedness of the market economy. In fact, such awareness was the very reason for establishing the Council in the first place. The question is, of course, how such awareness can be translated into operational rules for corporate management in a competitive, transnational environment. To expose companies as visibly as possible to the concerns of stakeholders will be a necessary condition. In the IPR case, the challenge is to devise business strategies and use legal rights in such a way that they strike a fair balance between the need to protect intellectual property and maximize return on investment, on the one hand, and the need to provide access to new knowledge and distribute the benefits of innovation to the society—especially the developing countries—on the other.

2. The Process: Deliberations with Stakeholders

IPR issues are discussed in numerous formal and informal arenas. The WBCSD project was specific, in that it convened conflicting parties in a sustained effort to sort out views, positions, and options through dialogue. While "dialogue" is the accepted norm in dealing with embattled political questions, it is seldom the social reality. In most settings the parties lack the time or capacity, or mandate to engage in extended deliberations over the arguments put forward. The WCBSD project intended to break that pattern, in keeping with models provided by previous projects such as the Keystone Dialogue or the Crucible Group.[2]

The IPR Dialogue Process involved some 50 participants: representatives from companies and civil society organizations, experts on IPR, and a number of

2 See, for example, The Crucible Group: People, Plants, and Patents—The Impact of Intellectual Property on Trade, Plant Biodiversity, and Rural Society, IDRC, Ottawa 1994; or, The Crucible II Group: Seeding Solutions, Vol. 1: Policy Options for Genetic Resources, IDRC, Ottawa 2000, and Vol. 2: Options for National Laws Governing Control Over Genetic Resources and Biological Innovations, IDRC, Ottawa, 2001.

observers from international organizations or governmental bodies. It included two face-to-face meetings, one conference in the beginning to decide the agenda and the rules of the Dialogue (Montreux, May 2001), and one conference towards the end (London, February 2002) to discuss the contents and procedure for drafting the final report of the project. Communication before, during, and after the conferences proceeded via internet exchange.

Communication through the internet was vital for the project. Without it, efficient cooperation of participants from 15 countries around the world would not have been possible. The Montreux conference gave the mandate to organize and moderate the internet exchanges and conferences to a team of scientists from the Social Science Research Center Berlin (Wissenschaftszentrum Berlin fuer Sozialforschung) (WZB).[3] The WZB team was expected to provide surveys of arguments on the topics that the participants put on the project agenda. Moreover, the members of the team screened the transactions of the Working Groups that dealt with these topics at the first conference, and analyzed related documents and literature proposed by the participants. The surveys of arguments were circulated back to the participants for response, further questions, and criticism. The responses, in turn, were synthesized and presented to the participants to be discussed at the London conference.

This procedure gave the WZB team a major role in preparing and supporting the deliberations throughout the project. Such a role was indispensable in view of the complex issues and interactions that had to be managed within the time scheduled for the Dialogue. It was understood that the WZB team would guarantee transparency of all transactions, and act according to the rule that full control over the Dialogue process rest with the participants. This rule implied, in particular, that the participants decide what to include in a report from the project, or what to add to such a report as commentary or dissenting opinion.

Formal supervision of the Dialogue process was exercised by a Steering Committee established by the participants at the first project conference in Montreux. The Steering Committee was in charge of organizing, compiling, and editing the final project report.[4]

3 The WZB team included: Wolfgang van den Daele, Rainer Döbert, Achim Seiler and Jost Wagner. At the London conference Michael Lesnick and Heather Lair (Meridian Institute, Washington) acted as a facilitators.

4 Project Steering Committee: Carlos Correa, University of Buenos Aires; Thomas Cueni, Roche Pharmaceuticals; Wolfgang van den Daele, Social Science Research Center Berlin; Johnson A. Ekpere, University of Ibadan, Nigeria; Maurice Iwu, Bioresources Development and Conservation Programme, Burkina Faso; Achim Seiler, Social Science Research Center Berlin; Patricia Solaro, Aventis; Ross Stevens, World Business Council for Sustainable Development.

STEPS IN THE IPR STAKEHOLDER DIALOGUE PROCESS*

March 2001	Framework for a Stakeholder Dialogue Proposed by the WBCSD
May 2001	First Conference (in Montreux, Switzerland)
Up to February 2002	**Circulars to the participants** (surveys of arguments from the First Conference and related documents)
	Responses to the circulars
	Synthesis of responses to the circulars and points to consider for conclusions
	Steps towards conclusions (proposals to be considered for the final report at the Second Conference)
February 2002	Second Conference (in London, United Kingdom)
Up to July 2002	Proposals for the Final Report based on the proceedings of the London conference
	Responses to the proposals, revisions, additions, dissenting opinions
July 2002	**Final Report** of the Dialogue Process to the WBCSD

*Documents indicated in bold are included in this report insofar as they relate to HRG.

3. The Product: Conclusions on the Access to Human Genetic Resources from the Final Report to the WBCSD[5]

The following pages contain an excerpt from the Final Report (July 2002) of the IPR Stakeholder Dialogue (part 1, "Access to Human Genetic Resources"). The footnote numbers in this excerpt correspond to the numbers in the original text.

5 World Business Council for Sustainable Development (ed.), Intellectual Property Rights in Biotechnology and Health Care—Results of a Stakeholder Dialogue, July 2002. This document is available from the WZB and the WBCSD (4 chemin de Conches, CH-1231 Conches-Geneva, Switzerland). It can also be downloaded from the respective websites: see <http://www.wz-berlin.de/ipr-dialogue/> or <http://www.wbcsd.org/> (under the rubric "Publications and Reports").

Access to Human Genetic Resources

Human genetic research is becoming a key resource for the development of effective new medicines. Accordingly, pharmaceutical companies have a vital interest in knowing under what conditions such research, if pursued in a business context, would be regarded as legitimate and accepted in the society. What rules should companies apply in collecting and storing data and samples from a large number of individuals? To what extent should pharmaceutical companies claim exclusive rights to use the data and sample collections? What is the proper scope for intellectual property rights on research results, on the road to development of the commercial product?

The participants of the *Stakeholder Dialogue Process* addressed these questions in their deliberations. Main conclusions are summarized under three headings:

- protecting the autonomy and the rights and interests of research subjects (informed consent, benefit sharing)
- balancing private and public uses of data and samples collected by companies (research consortia, access to databases)
- calibrating intellectual property rights (gene patents)

A. Protecting the Autonomy, Rights, and Interests of Research Subjects: Informed Consent and Benefit Sharing

(1) Background and Contexts

The principle of informed consent (IC) is unchallenged. Views differ, however, with respect to the regulations this principle implies. Industry tends to take a formal rule-of-law view that emphasizes the autonomy of the research subjects. Accordingly, it should be the choice of the subjects to say "yes" or "no" to the conditions of the research relationship: for instance, whether or not to demand benefit sharing, allow data and samples to be stored after a research project ends, or give broad consent to future projects. Stakeholders, in contrast, tend to take a substantive political view, emphasizing the contexts of power relations and inequality within which research subjects take decisions. From their perspective, IC is not just the acknowledgment of autonomy, but foremost a mechanism that empowers the weak to resist the strong. Accordingly, no decisions should be accepted by which research subjects give away control or do not use the options for control extensively.

In part, this difference may be more one of degree than of principle. After all, existing regulations do both: they acknowledge and strengthen subjective choice, and they impose some "objective" normative order that restrains choice. However, the difference is more profound. It makes it difficult to provide guidance for companies through a set of accepted rules that demarcate legitimate corporate behavior. Stakeholders tend to emphasize the need to take the social contexts into account, within which such rules should operate. Thus compliance with accepted rules will be essential; it will provide legitimacy only to the extent that the rules are perceived as constituting proper safeguards against the risks of genetic research and against the asymmetry of power and the hegemony of culture that prevails in the society.

1. *Building a Trust Relationship*. Companies should take special care to demonstrate that the relationship they seek with the research subjects will be equal and fair and based on mutual respect. Companies need to demonstrate that the presumptions of mistrust are unwarranted, which are widely held in society because of the inequalities in terms of power and information between companies and research subjects.

2. *The Ethical Order of the Research Relationship.* Respect for autonomy is the most important principle for the protection of research subjects, but it is not the only yardstick of a legitimate research relationship. For example, the Helsinki Declaration determines that subjects cannot give consent to research that involves them in unreasonable risks. There are rules beyond informed consent that constitute the ethical order of the research relationship, and these must not be violated—even if the subject agrees. Companies should be particularly committed to these rules and possibly amend them with a view to giving additional legitimacy to research in the business context.

3. *Protection against Social Risks of Genetic Research.* The future uses of the results of human genetic research in the society cannot be determined and monitored within the research relationship. However, the research will only be accepted if people can reasonably expect that misuse of the results and social risks from genetics will effectively be controlled in the society. Companies should support legal regulations that control such risks: data protection, anti-discrimination legislation, etc.

4. *Value of Genetic Research.* The *Dialogue Process* proceeded from the assumption that human genetic population research, if properly designed and controlled, may be valuable and in fact desirable, not only for the companies, but also for the society. While this premise was generally accepted, stakeholders pointed out that some communities could decide to opt out of such research as a matter of principle. It was acknowledged that communities have a right to do so, according to community rules, whenever the decision to participate in the research is a group-level decision. It was also accepted that (notwithstanding the requirement of individual consent) the basic decision of whether or not access to human genes should be granted for research belongs to the society at large.[3]

(2) Informed Consent (IC)

5. *Genuine Consent—the Right to Say "No".* All parties in the *Dialogue Process* agreed that genuine consent by the research subjects is a precondition for including their data and samples in the research. The modalities of "consent" must be determined from the cultural perspectives of the subjects, i.e., on the basis of their perceptions and values, not from the professional framework of the researchers. Subjects must be completely free to say "no" to the research, and no attempt should be made to coerce, manipulate or "buy" them into participation.

3 It was pointed out as a problem that ethical objections which are culture-specific could block access to human genes that might be beneficial for human health in general. The solution seems to be that in such a case the requisite research is shifted to countries that do not object to access to human genes for moral reasons.

6. *Explicit Consent—the Need to Opt In.* Public interest may justify exemptions from the requirements of IC. National legal regulation and professional tradition allow researchers, in certain cases, to draw on personal (identifiable) data and samples of subjects without consent or with reference to presumed consent. Companies should not use any of these exemptions for research in the business context. Rather, they should commit themselves unequivocally to the principle of explicit consent. They should always ask participants to opt into the research and not be content with the provision that participants can opt out—even if national law permits such an approach.[4]

7. *IC and the Use of Databases.* Companies should not use databases that collect personal data and samples without explicit IC. Exemptions from IC, which may be justifiable in the public interest, should not be exploited for private research.

8. *Withdrawal of Data and Samples.* The Helsinki Declaration rules that subjects in medical research can withdraw their participation at any time. The right to withdraw is an element of the ethical order of research with human subjects, and it cannot be renounced in IC. Companies emphasize that the rule fully applies when subjects contribute their personal data and biological samples. Subjects should, however, be free to authorize the anonymization of the data, or the uses of samples that make withdrawal unfeasible in terms such as their incorporation into secondary products.

9. *Sharing Samples and Data.* Anonymous data and samples incorporated in further products cannot be withdrawn. Data or samples shared (with consent) with research partners can, however, be withdrawn as long as they are identifiable.

10. *IC for Commercial Uses.* Companies shall disclose the commercial uses they envisage for the data and samples collected, and get IC for such use. Disclosure shall include the intention to develop secondary products (e.g., cell lines) from samples and to claim IPRs (patents) for inventions derived from the research based on the collected data and samples.

11. *Unforeseen Purposes of Research—Re-Consent.* If data and samples are to be used for other purposes than those agreed upon in the IC process, companies should always go back to the subjects and ask for new consent, unless data and samples were anonymized with the initial consent.[5] But it is acknowledged that the administrative burden of obtaining re-consent could be minimized by allowing consent for circumscribed areas of disease.

12. *Collected Data—Storage and Use.* Collections of (non-anonymized) data and samples constitute valuable resources for future research. Therefore companies should, with due consent, be allowed to store them over a longer per-

4 One participant from industry expressed the desire to have uniform IC requirements, i.e., irrespective of whether research would be undertaken by public or private organizations. Another participant from industry endorsed the above statement for the future but considered it inappropriate if industry uses data (or samples) it has legally obtained under a presumed consent rule in the past. In those cases industry should not be obliged to seek explicit consent from the subjects retroactively.

5 The proposal made by a participant from industry, to confine the need for re-consent to a period of, say, ten years, was not widely accepted.

iod.[6] However, the use of the stored data and samples may be blocked under the requirement of re-consent, if subjects can no longer be retrieved or if they are deceased.[7]

13. *Anonymous Data and Samples.* Data and samples anonymized with consent may be stored and used without restrictions, within the rules of law and the provisions of the competent ethical review committee.

14. *Broad Consent—Purposes of Research.* If the research projects for which data and samples are supposed to be used cannot be fully specified at the time when consent would be requested, the subjects cannot, strictly speaking, become fully informed. Participants concluded that subjects could nevertheless give consent in such cases, if they feel that they have sufficient trust. The crucial point is that consent must be genuine and emanate from the value system and assessment of the subjects, not of the researchers. Subjects may, for instance, decide whether or not to agree with the use of their data and samples in future research for circumscribed areas of disease. Such consent avoids blanket authorization for unlimited purposes, on the one hand, but reduces the administrative burden to obtaining re-consent, on the other. All future research projects have to be evaluated by appropriate ethical review bodies.

15. *Research in DCs.* Companies from the North should be particularly careful in research projects not to take advantage of poor, uninformed local people from the South; they should not, however, as a matter of principle, abstain from doing research in the South. As one stakeholder from the South put it, exclusion is now at the center of inequity, not exploitation. It is therefore important that decent and transparent research relationships with local communities be established.

16. *Community Consent.* Whether individual IC is sufficient to legitimize the collection of personal data and samples depends on the culture of the community. Traditional or indigenous communities tend to require approval by the group. Modern communities tend to leave the decision with the individual, within the confines of legal regulations. When community consent is required, its refusal overrides the consent of the individual to participate; but community approval is not a substitute for the lack of individual consent.

17. *Groups Affected by the Research*. It was discussed whether groups who could possibly be affected by the outcome of the research should have the right to authorize and, if they deem it necessary, to veto the research. In this case the need to negotiate IC would be extended to a large number of groups (patients, gene carriers, age groups, ethnic groups, persons seeking insurance or employment, etc.) who do not form a community proper and have no mandate to speak for, and act on behalf of, the research subject. The participants of the *Dialogue Process* felt that the legitimate concerns of such

6 One stakeholder requested, instead, that all data and samples should, as a rule, be destroyed once the agreed upon research has been accomplished.

7 One participant suggested that in this case the data and samples might still be used if they were removed from the exclusive realm of the company and placed under the rules and controls of public research.

groups should be addressed by legal regulation, but not by including them in the consent requirement.

18. *Community Consultation.* It was considered appropriate, however, that companies consult with groups in the society that may possibly be affected by the consequences of the research and, eventually, support demands for regulations that protect these groups.[8]

19. *Ethical Review.* Industry acknowledges that all research that draws on the collected data and samples should be reviewed by an ethics committee to make sure that the relationship with the subjects of research is balanced—i.e., that the research design complies with the stipulations of the IC and with general rules that may apply. It is understood that such committees should be independent and include genuine third parties not associated with the company. Approval by an appropriate ethics committee may be taken as a kind of community consent.[9]

20. *Social Risks of Genetic Research.* Social risks of genetic research and the question whether genetic research should be allowed must be dealt with through societal regulation. Beyond such regulation, individuals (and communities) can refuse IC if the research, according to their own assessment, implies unacceptable social risks. It remained unresolved in the *Dialogue Process* whether or not social risks must be disclosed in the IC process, and whose standards researchers must apply in order to decide what they have to disclose.

(3) Benefit Sharing (BS)

Questions regarding BS with human subjects involved in genetic research can trigger responses in which, paradoxically, the parties change sides: Companies may appeal to altruism, and they may frame participation in research as cooperation for the production of a public good (even if that good would eventually be achieved through commercial development); stakeholders, in contrast, may emphasize the economic self-interest of donors, and they may find acceptable the commodification of data and samples, as well as a business perspective on research participation. In the *Dialogue Process* there was some convergence (legal restraints such as those imposed by the Convention on Biological Diversity notwithstanding) on the idea that research subjects should be able to decide whether they want BS or not.

21. *BS—Control of Data and Samples.* Negotiations over BS must start from the principle that research subjects have control over their data and samples. Accordingly, the subjects must decide whether, and under what conditions, the data and samples can be used.

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8 One participant from industry argued that community consultation should not be a general policy with every single research project. Rather, the ethical review body should advise the company when to seek community consultation.

9 One participant pointed out that ethics committees, if they cannot rely on existing regulations, might apply ethical standards that are highly controversial in modern societies. In such cases, companies may consider the review as not binding. They should, however, expose themselves to the discussion invoked by such review.

22. *BS—Diversity in Culture Matters.* It was a common understanding in the *Dialogue Process* that whether or not individuals or communities participating in research should demand BS is an issue that must be decided upon according to the cultural values and orientations of the individual or community.[10]

23. *No One-Size-Fits-All Model.* Except for regulations that make BS obligatory (such as the Convention on Biological Diversity in the case of non-human genetic resources), the question of BS is largely a matter of negotiations during the IC process. Companies may to appeal to altruism and ask for participation in research as a gift, even though the goal is a commercial product. On the other side, subjects may regard such participation as a business relationship and pursue their own financial interests.

24. *Prevent the "Buying" of Subjects.* Most participants, representatives from industry and stakeholders alike, warned that turning research participation into a commodity undermines IC and leads to "buying" the consent of subjects. Especially under conditions of poverty, the offering of monetary incentives or other material benefits might amount to coercion.

25. *BS to Ensure Freedom to Operate*. Since companies want to ensure freedom to operate they are reluctant to enter BS arrangements that grant financial reach through claims on future rights and profits derived from the research. In addition, it is virtually impossible to quantify the extent to which such rights and profits might be attributed to the contribution of single research subjects. There are, however, also cases in which companies want to offer financial rewards in exchange for specific contributions from subjects regarding their rights over data or samples. Either sort of arrangement should be considered as possible and negotiable, provided that there is genuine consent and that the deal is not ethically objectionable—a matter, which, in any case, would have to be attested to by an ethical review committee.

26. *Indirect Benefits*. It was admitted that new drugs, scientific progress, and economic growth flowing from the research provide individuals (and communities) who participate in the research with some indirect benefits. It was also pointed out, however, that such benefits are less likely to accrue if the community from which the data and samples are retrieved is not the community in which the commercial development and production takes place. Thus special issues of equity and BS arise when Northern companies pursue research with subject populations from the South or from indigenous communities.

27. *Non-Monetary Benefits.* Companies and research subjects can (and sometimes do) negotiate BS in terms of preferential access to the products (diagnostic or therapeutics) that will be derived from the research. In North-South relationships, especially with indigenous communities, such BS schemes are advised as good practice, because the subjects and their communities would

10 One stakeholder held, however, that research participation without BS is unethical.

normally not be included in the flow of indirect (scientific and economic) benefits from the research activities in which they participate.[11]

28. *Gift Relationship and Pricing Policies.* The gift culture of providing data and samples for research is based on the understanding of the subjects (echoed by the companies) that they will contribute to the public good of medical progress, even though the research is declared to be for the development of commercial products. This understanding will quickly erode if the products prove to be unaffordable for the subjects or their families or patient groups to which they belong.

29. *Negotiating Pricing and Licensing Policies.* The participants in the *Dialogue Process* discussed some recent cases in which unreasonable prices where sought for genetic tests developed from research with human subjects. They proposed that subjects negotiate, and companies offer, arrangements that exclude such pricing policies. While, in general, it may seem difficult for companies to have their pricing policies discussed in negotiations with research subjects, such arrangements may only commit the companies to those policies which they advertise publicly anyway.

B. Balancing Private and Public Uses of Data and Samples Collected by Companies: Research Consortia and Access to Databases

(1) Research Consortia (RCs)

The Working Group discussed RCs that are explicitly designed to release their results to the public domain. The prime example in the discussion was the SNP consortium. While the participants agreed that such RCs might be feasible and useful, they differed in the interpretation of their significance and preconditions. Stakeholders tend to welcome these RCs, because they enlarge the public domain and restore a balance between private and public knowledge, which, in their view, is increasingly being upset by a race among industry and universities for patents on basic genetic information and research tools, far ahead of product-related inventions. Industry, in contrast, views such RCs as a pragmatic approach to distribute and reduce the costs and risks of research in areas that they consider pre-competitive. They may also be in favor of shifting certain knowledge to the public domain, because that preempts the patenting of the knowledge by competitors. However, industry sees no general need to rebalance the private-public relationship. They trust that excessive patent applications will be turned down by the patent offices anyway, and that, despite patent protection, research tools will be available on reasonable licensing terms.

30. *Companies Should Explore their Flexibilities.* The participants of the *Dialogue Process* agreed that RCs that release their results to the public domain or make them otherwise generally available might be a viable strategy to advance the knowledge in complex fields of genetics. The participants therefore encourage companies to explore the flexibilities they may have to engage in such RCs.

11 Some stakeholders argued that such BS should be extended to all subjects and communities involved in the research of the company not just to those who happen to provide data and samples that lead to successful developments.

31. *Viability of RCs.* RCs that release results to the public domain are a viable option, only if such release is compatible with the proprietary interests and conditions of companies, especially with the need to justify and protect the investment in the research.

32. *Different Company Schemes.* Admittedly, different companies may have different flexibilities. Small start-ups that use patents on research tools to raise money on the venture capital market will have fewer options to join RCs that release results to the public domain than will large companies that develop end-products for consumers.

33. *RCs Address Public Concerns.* Whether the patent system functions well in the field of genetic research and development is a controversial issue. There are serious public concerns that basic knowledge at the frontiers of genetic science will be protected by patents and subsequently appropriated for exclusive private use. RCs that release results to the public domain are a perfect means to address these concerns. RCs will undoubtedly contribute to the legitimacy of claiming exclusive rights to inventions further down the line towards products.

34. *Public-Private Partnership in RCs.* Experience shows that companies also engage in RCs in the fields of structural and functional genomics, or proteomics, provided the research is still at a distance from product development. Governments (and charities) are encouraged to support joint public-private RCs, in order to increase the options to retain basic knowledge from these fields in the public domain. Companies will have to assess whether, in their view, the advantages of public support warrant the price that companies would then not be able to claim exclusive rights to use the knowledge generated within the RCs.

(2) Access to Databases (DBs)

A leading question in the discussions of the Working Group was whether special rules should apply for DBs built by private companies with public support. The case of the Icelandic Health Sector Database provided the starting point for these discussions. The participants acknowledged that the rules for access to such DBs must recognize investments made in order to have the DBs in the first place. On the other hand, they also acknowledged that access to DBs built with public support should be non-exclusive and cheap.

35. *DBs as Public Infrastructure.* DBs (including sample collections) built with public support should be accessible as public infrastructure, irrespective of whether the DB operates under schemes of public or private law. Public support could either mean public spending or authorizing the inclusion of data collected in the public sector, or granting an exclusive license to build up the database.

36. *The Principle of Non-Exclusive Access.* Access to such DBs should be granted, with due respect for privacy protection, on a non-discriminatory basis to anyone who has the competence to us it. Exclusive licenses to use the DBs should not be issued; they are hardly compatible with the function of the DBs as public infrastructure.

37. *The Case of Clinical Trial Data.* The principle of non-exclusive access to DBs built with public support was adopted by the participants for DBs to be used as research tools.[12] DBs for product proof (clinical trial data) may warrant a different rule.

38. *Fees for Access.* Fees for access can be appropriate to recover some of the costs for building and operating a DB. Such fees will, however, exclude users if they are too high. The first priority must be to ensure that the DB will be used as widely as possible to get maximum societal return from the investment in public infrastructure. Special allowances should be made for poor users from developing countries.

39. *Higher Fees for Companies.* In many cases, companies charge higher fees for access to DBs than do academic researchers. The participants regard this practice as acceptable. However, care must be taken, that the use and the usefulness of a DB is not obstructed by the pricing scheme.

40. *DBs Within Companies.* The participants encourage companies to ensure that their DBs are accessible for wide use in the society, wherever this is compatible with companies' proprietary imperatives. Companies could also consider the transfer of old collections, which otherwise would be lost or would never go into general use under public control.

41. *No Reach-Through Provisions.* Participants concluded that, as a rule, holders of DBs should not require (and the user should not accept) that, in exchange for access, reach-throughs be granted on results or rights the user may obtain from the results achieved by using the DBs.

C. Calibrating Intellectual Property Rights: Patents on Genes

Patents on genes are contested. The participants of the *Dialogue Process* could not resolve the controversial issues. While in some cases they had a common understanding of the issues raised by patents on genes, their approaches to these issues were vastly different. Representatives of industry tended to start from the existing frameworks of patent law and considered how these frameworks may be applied and/or (if necessary) amended to cope with problems. Stakeholders, in contrast wanted to take a broader perspective. They urged that alternatives to the patent system be discussed, and they challenged the notion that patents on genes are needed to reward invention and protect investment in the life sciences. No consensual conclusions were achieved in the discussion on basic positions in this controversy; however, at various points the parties found some common ground. Representatives of industry considered the possibility to modify patenting strategies to address some of the stakeholder concerns. Stakeholders, notwithstanding their rejection of gene patents in principle, acknowledged that there might be modifications which, in their view, are steps in the right direction.

The following sections try to capture both the divergence of opinions and the common ground found in the discussions. For the sake of clarity it should be noted that

12 A question discussed (but left open by the participants) is whether DBs that comprise results (publications) from publicly funded research should not also be accessible as public infrastructure.

the representation of industry in the *Dialogue Process* was biased towards large pharmaceutical corporations.

(1) Alternatives to the Patent System

The debate over whether patents should be granted is as old as the patent system itself. The discussion in the *Dialogue Process* on alternatives to patents echoed that debate. While representatives from industry emphasized that the patent system has emerged as the best solution to balance societal interests in the promotion and dissemination of useful information, stakeholders insisted that alternatives to the patent system are possible and necessary. No consensus was reached in this respect. However, the participants did converge in the opinion that patents do serve functions that would also have to be met, if alternative systems were in place: namely, to reward invention and provide incentives to invest in R & D.

42. *Criticisms of the Patent System.* Stakeholders saw the public debate over patents on genes as indicating a deeper crisis in the patent system. They see patents as pursuing a winner-takes-all model, which is at odds with the incremental and collaborative character of modern R & D processes. In the opinion of stakeholders, patents serve more to protect investment than to reward invention; and stakeholders hold further that patents restrict the freedom of research and block innovation. Therefore, stakeholders call for alternatives to the patent system to be devised and implemented.

43. *Adaptive Capacity of the Patent System.* Representatives of industry argued that the patent system has worked well in the past and that it is the most appropriate legal system to balance investment risks, rewards for creativity, and early disclosure, in order to advance progress toward inventions benefiting the public.[13] Without the patent system, private investment in R & D, for example, for new drugs, could not be mobilized. Questions that might arise in the context of patents on genes could be addressed through adaptation within the patent system.

44. *The Need to Protect Investment.* Stakeholders acknowledged that companies have to make a profit, but that, if alternatives to the patent system were sought, then alternative models of financing R & D would be required.[14]

(2) The Moral Aspects of Patents on Genes (GPs)

Among the objections raised specifically against patents on genes, moral arguments are the most basic. There are strong voices in the public debate claiming that patents on genes should not be granted as a matter of principle, because GPs violate the moral order. However, there is no consensus among the societies with respect to the

13 One participant (industry) argued that there is no statistical evidence that the patent system has a negative impact on scientific dynamics of research and on the rate of innovation in industrialized countries. One possible comment to this argument is that aggregate data will not account for and accordingly miss single cases which may nevertheless be significant. Thus, there seems to be a need for detailed empirical studies, see also statement no. 57.

14 One idea that came up in the discussion was that the whole R & D chain for new drugs be transferred to (and financed by) the public sector, while private companies be confined to the production of the drugs. The proposal was not discussed at length, but there was a common understanding that alternatives to the patent system would imply major revisions of existing legal, institutional, and allocation arrangements.

moral standards that ought to apply. In the *Dialogue Process*, representatives of industry referred to existing patent laws and court rulings. They pointed out that claims for (human) genes are not comparable to claims for human reproductive cloning or producing human-animal chimeras—examples of inventions, the exploitation of which is considered immoral under the European Directive (Art. 6-2). Further, representatives of industry held that patents on genes could not offend human dignity, because GPs do not confer any ownership on individual human beings. In contrast, some stakeholders applied a broader moral framework. For them, granting exclusive rights to components or structures of life would constitute a serious devaluation of life and an improper way for humans to relate to nature. Therefore, they consider patents on genes to be fundamentally wrong. The participants in the *Dialogue Process* disagreed over these issues, but they agreed on some features and implications of their disagreement.

45. *Acknowledgement of Moral Diversity.* The participants in the Dialogue Process disagreed as to whether patents on genes contradict moral rules. They acknowledged, however, that this disagreement reflects the diversity of moral views in the society. People draw the lines differently: for some it is obvious that patents on genes constitute a breach of morality; for others this is clearly not the case.

46. *Moral Coercion Through Majority Rule.* Participants also acknowledged that legal rules allowing genes to be patented offend the beliefs of those who object to such patents for moral reasons, and, further, that these individuals may find it coercive to have to live in a society that grants such patents. However, such coercion is common in modern societies; it follows from the principles of democratic majority government. For example, in many countries, people who object to abortion for fundamental moral reasons must nevertheless live with the fact that the practice of abortion is spreading in the society.

47. *Public Rules and Personal Moral Views.* People should not be obliged to violate their own moral beliefs. However, this principle does not yield a right to dismiss public rules, even if such rules are seen to be in conflict with personal moral views. Normally, individuals can only choose, within their own private sphere, to dissociate themselves from practices that they consider immoral. Thus, they may decide, for instance, not use products based on gene patents. However, they cannot ignore the legality of such patents. A different conclusion would only be warranted if basic human rights or key elements of the rule of law were at stake.

48. *Evolving Moral Frameworks.* While some stakeholders insisted that, for them, patents on genes raise fundamental moral issues of how humans should properly place themselves in nature and how they should deal with life, it was generally acknowledged that such moral tenets do not have the status of basic human rights. It was, however, also accepted that moral frameworks are dynamic in modern cultures. Discussions over patents on genes will continue. Should a predominant view evolve that such patents indeed violate morality, then the laws allowing such patents will certainly have to be reconsidered.

(3) Policy Aspects of Calibrating Patent on Genes

Many of the arguments challenging patents on genes are not on the level of fundamental moral concerns: rather, they invoke policy considerations of how invention can be properly rewarded and innovation promoted, how a balance can be struck between exclusive rights and open access. Stakeholders in the Dialogue Process, while underlining their rejection of patents on genes in principle, involved themselves in discussions over the more pragmatic questions of whether companies do in fact need patents on genes to protect their proprietary interests, and how the scope of such patents should be calibrated—and possibly restricted.

In view of the fact that patent legislation is still pending in many countries, and that few court rulings have been issued to clarify the scope of protection granted by patents on genes, the discussions focused mainly on rules (and interpretation of rules) *that the companies could live with*. While one representative of industry pointed out that companies (like everybody else) occasionally defend what they have and consider the maximum protection they can get as a functional necessity, others emphasized that this is not the general attitude. Representatives of industry agreed with the need to acknowledge differences of opinion, have a dialogue, and find compromise.

The discussions in the *Dialogue Process* revealed some flexibility, as is reflected in the following statements.

49. *Controversial: The Need for Patents on Genes.* There was no consensus over whether patents on genes are necessary to provide the R & D investments needed for the invention of new medicines. Representatives of industry disagreed with the position that patents on end products are sufficient; patents on intermediary results (research tools), such as drug targets, may well be essential. Also, in their view, other mechanisms that protect investment in research, such as exclusive rights on clinical trial data or orphan drug regulations, cannot always substitute for patent protection on research tools.

50. *Scope of Patents on Genes.* All participants acknowledged that patents should only be granted for inventions, not for discoveries. There was consensus that this rule excludes patents on genes per se in their naturally occurring state. However, representatives of industry did not accept that genes isolated from their natural state and purified should also not be patentable as a rule. Instead they held that the European Directive struck an appropriate compromise ruling that mere DNA sequence information without indication of a function is not patentable, but that patents can be filed if the gene function and a utility/industrial application (for example, as a drug target) is specified.

51. *Legal Perspectives.* Participants from industry pointed out that one can only determine with certainty the scope of patents on genes after the appeals courts have clarified the meaning of the statutory requirements. Representatives of industry envisaged the possibility that European law might require that the gene function be indicated in the patent claims, and that this requirement could potentially limit patent protection to the function dis-

closed. Some representatives from industry conceded that they could live with such a rule.[15]

52. *Patents on Genes Must Not Restrict Freedom of Research*. All participants proceeded from the premise that patents on genes must not be used to bar access to building blocks of science or to research tools. Industry, however, argued that, in fact, no problems exist in this respect, because research tools are often available at a reasonable price, or that research exemptions exist in many countries allowing the use of patented knowledge under specific conditions. In addition they emphasized that it is the policy in many companies to license research rights generously and not to litigate against researchers in academic institutions.[16] However, problems may arise nevertheless, since research exemptions only allow for experimenting *on* an invention, i.e., testing, but not *with* an invention, i.e., the use of the subject matter for the purpose for which it had been developed. Accordingly, such a "use" would necessarily conflict with the exclusive rights of title-holders. In this regard, the group acknowledged the need for the development of a "fair experimental use" — doctrine which addresses especially the issue of research tools.

53. *Safeguards to Protect Freedom of Research.* An underlying expectation in this discussion was that companies should pledge to make the goodwill policy of granting access for research purposes a stable and sustainable pattern. It was understood that strong research exemptions are needed to underpin such commitment, and that options for compulsory licenses to guarantee freedom to do research should be available if companies are uncooperative.

54. *The Balance With the Legitimate Concerns of Inventors.* On the other hand, the principle of freedom of research cannot authorize unlimited use of inventions. There is still the need to balance the interest to facilitate access to research tools with the need to provide a fair amount of control/exclusivity to the inventor, because of the effort, time, and investment risk undertaken by the inventor. In general, patentees will find it easier to provide access to proprietary technology, if the use is truly restricted to research or at least to a use within a developing country where there would be no export of products.

55. *Coping with the Patent Thicket: Licensing.* Representatives of industry argued that there is no reason, nor any convincing evidence to assume that patents on genes will block innovation. While broad patent protection may mean that one has to get a license for any dependent innovation that uses the gene (even if the innovation is unrelated to the utility disclosed in the original gene patent), licensing and cross-licensing are said to be normal and adequate instruments to cope with the patent thicket. They also pointed out that patents on genes are unlikely to block the commercialization of downstream

15 One participant from industry proposed that the following statement be made: "Representatives of industry envisaged that European law will require that the gene function be indicated in the patent claims, and that this requirement will limit patent protection to the function disclosed. They indicated that this interpretation is seen as appropriate."

16 One participant from industry proposed that the last three sentences be replaced with: "Representatives of industry, however, argued that, as one of its seminal and intentional aspects, patenting forces the dissemination of knowledge that otherwise may not be disclosed, and that no patent restricts research. Thus, patents foster additional innovation and research rather than inhibiting it."

innovation, because there is a trend among patent-granting authorities to narrow down claims so as to prevent undue restrictions of follow-up inventions.

56. *Unwanted Corporate Strategies.* Industry acknowledged, however, that there are cases in which companies charge prices for patented technology, for example, for genetic tests, which may in fact mean that the technology cannot be widely used. They also acknowledged that dependent patent holders could not expect that cooperation on reasonable terms could be achieved in every case. Some companies demand royalties that are clearly unacceptable.[17]

57. *Empirical Questions.* Participants agreed that it was desirable to collect more empirical data on the practices of licensing and cooperation that evolve around gene patents, in order to determine whether or not problems of access to research tools and blocking innovations exist.

58. *The Option for a Compulsory License*. Participants agreed that legal safeguards are needed to protect the freedom of innovation. Holders of dependent patents should be able to seek a compulsory license for improvements if they cannot reach a deal with the holders of gene patents.[18]

(4) Special Protection of the Interests of Developing Countries (DCs)

The effects of patents on genes on DCs were a key concern of stakeholders in the *Dialogue Process*. Stakeholders argued that GPs exclude DCs from access to new technology. Representatives of industry pointed out that few gene-related patents are filed in DCs, and even fewer granted. In their view access to new technology is inhibited through lack of resources and infrastructure, rather than through exclusive intellectual property rights. The companies emphasized that they have no interest in blocking research in DCs, and that they are willing to collaborate through licensing or joint ventures. While patent protection by definition imposes restrictions on the access to protected technology, it remained an open question in the discussion whether, or to what extent, DCs are particularly at a disadvantage through such protection.

Some representatives from industry pointed out that it is to the advantage of DCs to implement appropriate IPRs in order to promote a fair equilibrium between Industry and DCs and to guarantee the recognition of DCs' innovations. India's (starting) pharmaceutical industry, which is clearly pro patenting, provides a good example.

Some stakeholders took the perspective of indigenous communities and argued that the extension of patent protection driven by the WTO/TRIPS framework constitutes injustice *per se*. They held that the extension of patent protection replaces traditional systems of intellectual property, for example collective ownership-of-knowledge schemes implied in customary law, and that it deprives indigenous communities of the right to operate under their own cultural, social and legal values.

17 One participant from industry disagrees with the statement and proposes the following amendment: While it could be acknowledged that access to patented technologies "(as in all other walk of life) is limited by their affordability[,] providing such access and affordability is, however, a societal issue that, for the most part, is subject to the same free market framework as all other commercial activity."

18 One participant from industry withheld agreement with the last sentence.

There were few lines of convergence in this discussion, but it was acknowledged that special safeguards should be explored which respond to the concerns voiced by representatives of DCs.

59. *Empirical Questions.* There was an implied understanding that more empirical investigation is needed to determine whether, or in what respect, DCs are disadvantaged through the granting of patents on genes. In particular, one needs to find out whether (and why) mechanisms that mitigate the exclusive effects of patent protection in the North may not work well in the South.[19]

60. *Support for Challenging Patents.* Experience proves that many patent claims fail if they are challenged in courts. However, high litigation costs and scarcity of legal expertise are hurdles for DCs, hindering their ability to legally challenge patents they consider invalid. Many participants, also from industry, acknowledged that some mechanisms should be introduced to help DCs challenge patents. An initial step might be compulsory public disclosure when a patent has been successfully challenged in any country, or a rule that allows abridged procedures in a DC in cases of the final invalidation of a patent in a Northern country. It is understood that such a rule would respect the defense rights of patent holders in appeal procedures.

61. *Discussion of New Ideas.* Representatives of industry agreed that it might be worthwhile to discuss new ideas for special consideration of DCs needs. The model of the FAO International Seed Treaty was cited in this respect. The treaty guarantees free access to important agricultural genetic resources included in a multilateral system, and limits the possibility to get patent rights on these resources. It could be explored whether a similar model might be developed for other genetic resources as well, on a case-by-case basis and through international agreements.

19 One participant from industry pointed out that it should also be investigated whether and to what extent cheap and rapid access of DCs to the patent system would counterbalance any disadvantage.

4. Discussion: Convergence and Divergence in the Deliberations of the Stakeholder Dialogue Process

This section gives a brief analytical review of the results of the stakeholder dialogue by the WZB team. It discusses the achievements and limitations of the cooperation of the participants in their deliberations on contentious issues of Access to Human Genetic Resources. The participants will, of course, have to give their own assessments of what they achieved or did not achieve. Our review also draws on the series of documents that have been created by the WZB team and distributed to the participants during the dialogue procedure. Excerpts from these documents are included in the Appendix (below); they may be consulted by the reader to gather additional insight into how the deliberations proceeded. It must be noted, however, that the Final Report presented by the Steering Committee (see previous section) is the only authorized text on the results of the dialogue procedure.

4.1. Premises for Compromise

Human genetics is perceived with ambivalence. It raises hopes for new medicines and fears of genetic discrimination, as well as ethical concerns about the manipulation of human life. This ambivalence was reflected by the parties in the dialogue. Companies and NGOs represented conflicting views, but they had sufficient common ground to cooperate in the deliberation over proper rules for human genetics research. The pharmaceutical companies accepted that they must build trust and address the public fears and concerns if they are to pursue the research legitimately in a business context and claim intellectual property rights on its results (1)[6]. The NGOs, on the other hand, accepted as a baseline for the discussion that the research could lead to new medicines and would therefore be of great benefit for patients (4). This baseline paved the way to compromise because it operated against any temptation to account for the fears and concerns by ever more restrictive rules, which, in effect, would amount to a complete ban on access to human genetic resources.

4.2. Informed Consent

Confirming the Standard Rules

All parties agreed that informed consent is a conditio sine qua non, if samples or data from human subjects are to be used in research. Consent must be genuine and reflect the cultural perceptions of the subjects and not the professional needs of the researchers (5). Researchers must disclose all intended uses, including the intention to claim IPRs on inventions derived from the research (10). The subjects may with-

6 Numbers in parentheses following statements in this section refer to the numbered points (1-61) in the excerpt from the Final Report contained in the previous section, 3, of this paper.

draw their samples and data any time, except in cases where these have been anonymized with the subjects' consent (8-9).

These principles were uncontested, but the participants differed about their political meaning. The companies considered informed consent as a means to obtain a legitimate "yes" to the collection and use of samples and data, whereas several NGOs looked at it primarily as a means to maximize the power of the subjects to say "no". The NGOs concern was that research subjects are highly vulnerable and likely to be abused because of the asymmetry of power and the hegemony of professional culture in research relationships. They nevertheless supported the standard rules. The NGOs admitted that respect for autonomy implies that subjects must have an option to say "yes". On the other hand, they accepted the rules as *necessary*, but not as *sufficient* conditions, and thus withheld final word on the legitimacy of the research.

Best Practice Rules

The pharmaceutical companies pointed out that they are determined to "go an extra mile" beyond the standard rules. They agreed not to take advantage of samples and data collected without consent or with reference to presumed consent, even if such collections have been authorized by the law (7-8). They acknowledged that under this rule they could not use the Icelandic Health Sector Database, which triggered heated public controversy, because it is to include health data from all Icelanders without explicit consent—subject, however, to a right to opt out.

The companies also acknowledged that they would seek re-consent whenever they intended to use the samples and data for purposes other than those specified in the original consent form (11-12). This implies that the companies would not use exemptions from the need for re-consent, even if such exemptions were legal and otherwise used. Apparently, the companies would rather forego some opportunities for research than put their own legitimacy at risk.

This commitment to a strict application of the informed consent principle can be read as a trust building policy. The costs of the re-consent rule were reduced in the dialogue by admitting that research subjects can give broad consent to future research, which is not yet fully specified (e.g., for certain classes of diseases) (14). The crucial condition is, as the NGOs pointed out, that research subjects have enough trust to grant such consent. The fact that all participants accepted this exception indicates a shared understanding that a balance must be found between optimal use of genetic resources in medical research and optimal protection of the autonomy of research subjects.

Requirement of Community Consent?

Traditional or indigenous societies may rule that individuals cannot dispose of their genetic samples and data without the approval of the group to which they belong. The participants of the dialogue concluded that such rules should be respected, and community consent be sought in these cases, in addition to individual consent (16). By implication, these communities have a right to ban all investigation of the genetics of its population.

In modern societies individuals can decide whether or not they want to contribute to research. Community consent is, so to speak, given through the legal framework which condones the right to choose, subject to some minor restrictions such as mandatory review by ethical committees. The participants discussed whether one could go further and give groups in the society (patients, ethnic groups, age groups, etc.) a say in research projects which those groups feel could affect them. The idea was not taken up. The main argument was, that most of these "groups" are not really social groups or communities, but rather analytical classes or sets of people who share certain properties (typically: age cohorts). These classes of people are not incorporated as collective actors and have not entrusted speakers with a mandate to act for them. Patient organizations can speak for their members, but not for the patients (17). The participants concluded that the companies should address concerns of people who are possibly affected by the envisaged research through community consultation (18). Consultations can involve patient organisations or other selective groups; they do not presuppose a representative mandate.

Should Social Risks Be Disclosed for Informed Consent?

This was the one question in which the standard rules of informed consent were not generally supported (20). These rules confine the duty to disclose risks to personal risks of the research subject. Several NGOs insisted that social risks must also be disclosed to enable subjects to reject research on the ground that it puts the society or groups in the society at risk. Other participants countered that arguments about social risks are usually contested, and that reliable information is scarce. The suggestion that research subjects should be referred to the websites of the critics of genetics was not accepted. The participants did not find consensus. They agreed, however, that social risks, which may result from the use or misuse of human genetic research, must be addressed by legal regulation, and that the companies should advocate such regulation (3).

4.3. Benefit Sharing

Commodification of Samples and Data?

There was consensus that it is unethical to "bribe" human subjects into the participation in research (24). Most participants also rejected schemes for benefit sharing with the subjects. The gift culture in which samples and data are donated to help science should not give way to a business culture in which they are sold to make money. Other participants, however, who were particularly involved with North-South issues, held that benefit sharing should be mandatory and that it was, in fact, unethical to receive samples and data without paying for them. The position of these particular participants was apparently inspired by the Convention on Biological Diversity (CBD) which requires benefit sharing for access to non-human genetic resources.

Most companies took a pragmatic stance in the dispute. They considered freedom to operate their first priority and were prepared to negotiate a price for samples and data if it were necessary for easy and legitimate access (25).

The discussions in the dialogue suggest that long-standing arguments against the commodification of participation in medical research are loosing ground. At least in a trans-cultural and transnational (North-South) setting the political and ethical assessments are ambiguous. Consequently, the participants concluded that it should be left to the individuals to decide according to their own cultural values whether or not they want to negotiate for a price in return for the samples and data they contribute (nos. 22-23).

The participants agreed that special issues of equity arise (and benefit sharing seems appropriate), when Northern companies pursue research with subject populations from the South or from indigenous communities (26). The underlying rationale was that these subjects are less likely to benefit indirectly from the research to which they contribute, for instance, through better health care (26-27).

Benefit Sharing with the Community?

Benefit sharing with a community may be required by law or stipulated by communities whenever they are partners in research contracts. The participants in the dialogue did not claim, however, that companies have a general moral duty to offer benefit sharing to the society when they negotiate the use of human samples and data in medical research for commercial purposes.[7] Taxation and regulation (including the possibility of price controls) remain as the proper means to redistribute benefits from companies to the society.

7 Such a duty has been stipulated by the Ethics Committee of the Human Genome Organization; see The HUGO (Human Genome Organisation) Ethics Committee, "Statement on DNA Sampling: Control and Access" <http://www.gene.ucl.ac.uk/hugo/sampling.html>.

Negotiating Product Prices and License Fees

The participants acknowledged that a gift culture of contributing to medical research will only be viable if the products of the research are affordable for those who contribute. They (cautiously) suggested that companies could commit themselves in research contracts to adapt their pricing and licensing policies accordingly (28-29). Whether robust commitments in this respect can really be expected, may be questionable, even though companies argue that in practice they act to assure that patients or groups who contribute to the research have access to the products of the research. Research subjects may increase their bargaining power by organizing in patient groups. Under certain conditions compulsory licensing could be an alternative approach.

4.4. Research Consortia and Access to Databases

Research Consortia to Release Results to the Public Domain

The Final Report encourages companies to explore the feasibility of research consortia (RCs) (30). The SNP (single nucleotide polymorphisms) consortium was considered as a model case, which could perhaps be extended to other fields of genetics. The participants acknowledged, however, that the model may not be economically viable once the research comes closer to the competitive areas of product development (31, 34).

Research consortia that place their results in the public domain were seen by some NGOs and experts in the dialogue as a means to reverse the tendency to obtain patents that restrict the free use of basic genetic information and research tools. RCs were also advocated as part of a broader vision that genetic resources should be defined as a common heritage of humankind and not appropriated under any exclusive rights. Although this vision resonated with the political preferences of a number of participants it did not become a topic for conclusions. Not only companies received it with scepticism, but also NGOs and experts who supported the CBD approach, which grants a right to control the access to genetic resources to the nation state.

Ensuring Access to Databases

The participants shared the understanding that genetic databases are important infrastructures for research, which should be used as widely as possible to maximize the scientific benefits to be drawn from them. They concluded that research databases built with public support should be accessible as public infrastructure, possibly for a fee, but on a non-exclusive basis (35-36, 38-39). It was understood that such rules reject the scheme of the Icelandic Health Sector Database which gives an exclusive license for commercial uses to the company that builds the database. On

the other hand, the participants were aware that investments to build the databases in the first place must be protected, and that it remains to be seen whether private investment to build a country-wide database can be mobilized without an exclusive license. The Estonian database project will perhaps provide a test case.[8]

The companies in the dialogue pointed out that they see options to make their own private databases accessible to other scientists. The Final Report encourages the search for such options, and urges companies not to claim rights on the results of other scientists' research in exchange for access to these databases (40-41). The Final Report also proposes that the possibility be considered that databases, which are not currently used by the companies, be placed under public control for general access.

4.5. Patents on Genes

Reformist Agenda Amidst Fundamental Controversy

Several participants argued that the dialogue procedure should deal with alternatives to the patent system as such, because the system had increasingly become dysfunctional as a means to promote creativity and innovation in the society (42). The deliberations discouraged such discussion. Even the critics admitted that alternatives to the patent system would also require alternatives for financing R & D (44), which could mean that drug development would have to be completely shifted from the private to the public sector. To consider these implications was outside the envisaged scope of the dialogue project.

The fact, that many of the critics were themselves professional experts in patent law contributed to the willingness to adopt the reformist agenda advocated by the pharmaceutical companies. These critics were interested in exposing malfunctions of the patent system, as they see them, and exploring options to cope with these malfunctions within the system (43). Others reserved their fundamental objections and at least did not reject the agenda. The same type of procedural compromise occurred in the discussion of patents on genes. Critics who opposed such patents as a matter of principle became nevertheless involved in arguments over the specific problem and possible solutions.

The Moral Objection Against Patents on Genes

The argument that patents on genes are inherently morally wrong was upheld in the dialogue procedure by several stakeholders. However, it was not framed in the rhetoric that is often used in public debates. The technical expertise in patent law brought to the discussion by both the companies and their critics in the dialogue operated against the plain language of "ownership of life". It was accepted, how-

8 The Estonian database may be a test case in this respect, see <http://www.genomics.ee>.

ever, that the moral objections may nevertheless be valid if, according to the cultural values held in the society, the granting of rights to control the use of genes for commercial purposes is considered to be an unacceptable devaluation of life.

Many participants declared that they could not share this objection—among them several of the experts and NGOs who had vigorously confronted the companies on other issues. The blurry lines of conflict probably helped the participants to acknowledge the existence of moral pluralism in this question (45). It was agreed—at least in the context of the dialogue—that there may be more than one morally acceptable position with respect to patents on genes, that democratic majority decision is legitimate, and that the granting of such patents cannot easily be equated with the violation of basic human rights (46-48).

No Interpretation of the Morality Exception Under Patent Law

The Final Report is silent about the question of whether unethical behavior during the research phase (e.g., access to genetic samples without informed consent, or theft of data) should constitute a case against the patentability of inventions derived from the research. This silence is in line with the standard interpretation of patent law (and TRIPS) which denies a patent only if the commercial use of the invention as such violates morality; the correction of flaws in the research leading to the invention is relegated to other legal remedies (damages or penal law). But the silence in the dialogue can hardly be interpreted as a general commitment to this interpretation. In the context of traditional knowledge, the participants concluded that the documentation of lawful and rightful access should be a precondition for the granting of patents based on the use of such knowledge (89).

The Dominance of Technical Experts

In the dialogue procedure, the political debate over the limits of gene patents was largely a representative technical debate between the experts of patent law from the side of the companies as well as the side of the critics. The reason for the dominance of the technical experts was that political debates usually make assumptions about what patents are and what their effects on the society will be. These assumptions are bound to be questioned in a deliberative setting; this implies reference to the expertise of specialists.

The deliberations dealt more often with controversial empirical assessments than with conflicts over values. Many normative issues were uncontested—for instance, that freedom of research must be preserved, that innovation should be promoted, and that developing countries should not be put at a disadvantage. The participants disagreed, however, as to whether, or to what extent, patents on genes do in fact lead to problems in these respects. They proposed that further empirical investigation be undertaken to assess those issues (58-59).

The participants disagreed over whether the isolation of genes always counts as discovery, or whether this technique is patentable as invention in certain cases; they also disagreed over whether patents on genes are fair and can be justified as compensation for the creative effort and investment made by the "inventor" (49, 50). These were clearly value conflicts, but they, too, had an empirical side. The parties shared the understanding that compensation is needed and justified to stimulate investment in R & D for new medicines. They did not share the assumption, however, that patents on genes are in fact necessary to that end.

Intervening Variable: Licensing Practices of Patent Holders

The companies frequently argued in the Dialogue that problems which can be associated with patents on genes in theory will not occur in practice because of proper licensing policies of the patent holders. The critics countered by pointing to cases in which no such policies had been applied. In line with the objectives of the stakeholder dialogue to explore what companies can do to avoid problems, it was suggested that proper licensing policies should be made binding, at least, as best practice codes to which the companies commit themselves in public. These suggestions were sometimes, but not always, taken up, presumably because the companies wanted to reserve the right to decide on a case-by-case basis.

Experimental Use Exception for Research Tools

The participants agreed that patents on genes and gene products (e.g., receptors) must not preclude the access to these genes (and products) as research tools in science. While the companies insisted that patents on such molecules, which may be drug targets, are essential for them (49), they accepted (with exception) the conclusion that companies should pledge to make the good will policy of granting access for research purposes a stable and sustainable pattern. And, they supported the idea that options for compulsory licenses to guarantee freedom to do research be available if companies are uncooperative (53).

The participants also acknowledged the need for a *"fair experimental use doctrine"* to deal with the question of whether one can do research *with* a (patented) gene and not just *on* the gene (52). The proposal came close to what is sometimes referred to as the "informal research exception", namely, that patent holders normally do not sue for infringements which occur in the setting of purely academic research. It was, however, also emphasized that free access to research tools must still be balanced with the legitimate interests of the inventors (54).

Addressing the Needs of Developing Countries

The participants acknowledged that developing countries must be helped to cope with the patent system, to ensure their access to new technology. The Final Report

concludes that special procedures should be put in place to enable developing countries to challenge patents they consider invalid (59-61).

The Range of Rules that Companies "Could Live With"

Companies insisted that patents on genes are needed to sustain private investment in R & D for drug development (49), but they were flexible with respect to the scope of such patents. Apparently, they did not see a problem with adapting to the new, more restrictive interpretation of the inventiveness and utility requirements recently introduced by patent offices, although the new interpretation will probably make most of the thousands of applications that have been filed for patents on gene sequences in the last decade obsolete (50, 55). Companies also indicated that they could get along with the rule of the European Directive that patents on gene sequences should not be granted without indication of the biological function.

Companies acknowledged that the interpretation of the statutory patent criteria by the appeals courts would probably add further restrictions to the scope of patents on genes, but they voiced no concern over this prospect. One representative even concluded that industry could live with the possibility that the European law might limit patent protection to the function disclosed (51). It was apparently inferred here that "function" refers to a biological level beyond the gene product and that this would be disclosed in the patent claim and not just in the description of the invention. In line with this assumption, it would be possible to cope with the "patent thicket" that troubles researchers who find that the genes (and gene products) with which they work are covered by broad product patents (55). Patent protection would be confined to the disclosed gene function and not extended to other (as yet unknown) functions. This conclusion, however, was not generally accepted by the representatives of companies in the dialogue procedure. Nevertheless the deliberations can perhaps be read as indicating that there is more flexibility over this point and more room for compromise than the usual public debates suggest.

As a final comment, it must be noted, however, that the participation of industry in the dialogue procedure was biased towards representatives the of big pharmaceutical companies. Small start-up biotech companies may be less willing to concede flexibility.

Appendix: Arguments from the Participants

The materials presented in this Appendix are from the Circulars on *Access to Human Genetic Resources (HGR)* prepared by the WZB and distributed to the participants for criticisms and comments during the dialogue procedure. The first of these Circulars proposed the following analytical scheme of the problem areas related to access to HGR, which was adopted by the Working Group:

Table: Problem Areas related to Access to HGR

Access to HGR and protection of the rights and interests of individuals or populations	Benefit sharing (BS) with individuals or populations who provide data or DNA samples	IP protection and exclusive rights for the use of the databases and research findings.
• Individual informed consent (IC) • data protection • Independent ethical review of research protocols • Community consent or consultation	• BS with individual subjects of research • BS with the community	• Freedom of research—access to databases • Exclusive licensing to do commercial research • Patenting genes • Research consortia (RC)

The Working Group dealt with most of these issues in recursive discussions organized by a series of Circulars marking the steps of the dialogue process (see p. 4 above). The Appendix summarizes the "Survey of Arguments" (including questions posed to the participants), the "Synthesis of Responses by the Participants", and the "Points to Be Considered for Conclusions".[9] These materials illustrate how the Dialogue proceeded to the point at which proposals for the Final Report could be drafted that where then discussed at the London Conference.

9 The documents can also be inspected on the WZB website <http://www.wz-berlin.de/ipr-dialogue/> (under the rubric "Dialogue Documents").

A. Informed Consent

A1 Survey of Arguments

The principle of IC is uncontested. Opinions differ on whether exemptions from the principle could/should be applied in certain cases. Traditionally such exemptions have been accepted for "retrospective" research that uses existing (anonymized or encrypted) health data and biological samples collected for other purposes than the envisaged research. The question is whether these exemptions should be extended to population research in human genetics. Controversy was, however, to a certain extent put at rest in our discussions because most industry representatives declared that it was the policy of their companies to minimize the use of such exemptions and require comprehensive IC in genetic research for all use of data and samples wherever the consent (and re-consent) is technically feasible.

Similarly we have seen some convergence of opinion on how the rights of patients and donors to withdraw from participation in the research can be guaranteed. Finally there also seems to emerge some common understanding of when and how community consent or consultation should be sought for genetic research.

In view of theses convergences the WZB team suggests going one step further in the dialogue process and testing some preliminary conclusions. Therefore, you will not find *further questions* at the end of every section but rather *proposed conclusions*. These conclusions refer to the following questions:

1. Is there a case for exemptions from the need to obtain informed consent when health data and biological samples are used in genetic research?

2. Should general consent for unspecified genetic research in the future be admitted/asked for?

3. Should IC have to disclose the possible risks of genetic research for the society?

4. Should IC have to disclose the possible commercial use and value of the data and samples provided?

5. Are there limits to the right of participants in medical research to withdraw samples and data?

6. Should not only individual consent but also community consent be sought for the use of population data and samples in genetic research?

7. In Search of 'Best Practice'.

(1) Exemptions from the need to obtain informed consent

Question: Is there a case for exemptions from the need to obtain informed consent when health data and biological samples are used in genetic research?

Main positions

Pro	Contra
• It is accepted practice that data (and samples) which have been collected for other purposes can be used in retrospective (epidemiological) research without informed consent if the research has been but approved by an ethical review board. The Icelandic Health Sector Database is in line with that practice. **[Arguments 4, 7, 8, 10, 12, 14]**	• Using health information from disease registries may be possible with presumed consent, if the data are anonymized. Linking identifiable health data with genealogy and genetic data should only be admitted with an explicit consent from participants **[Arguments 15, 22, 23, 24, 25]**
• Research on existing samples that are identifiable should be admitted after ethical review, if it does not exceed minimal risk to the donor. **[Arguments 14, 18]**	• In establishing databases and sample collections for genetic research companies should always obtain appropriate and explicit informed consent from patients that are enrolled in the research in respect to both samples and to data that are taken for this analysis. **[Arguments 27, 28, 30]**

Arguments

Issue	Pro	Contra
Arguments over the Icelandic Health Sector Database (HSD)	1. Informed consent for generating genetic data and for linking them to the medical information in the database is obtained at the time of blood collection form Icelandic volunteers. (Stefansson 1999: 30)	2. *[NGO$_1$]* The database act is an invasion of privacy … medical records of potentially every citizen of Iceland, dead and alive … [are] taken without asking. (M5/54-65)
		3. By making identifiable health information available without the consent of the patient the database violates the basic principles established to allow the use of (health information and biological samples) and at the same time uphold patient autonomy and dignity. (Zoëga et al. 1999:45/58)

Issue	Pro	Contra
Retrospective research with presumed consent	4. *[Industry$_4$]* Distinguish between prospective medical research … which is conducted on live people *[and]* retrospective medical research which is research on available data; not on people. Genetic research is prospective in nature; you have to approach an individual … to give you a blood sample. All of the genetic research deCODE is doing is done with individual written informed consent. Retrospective medical research … is traditionally performed with presumed consent. (M5/234/261/299)	5. *[NGO$_1$]* Taking the medical data without asking is justified with a nebulous concept of presumed consent … *[however]* this is really no consent at all but really the confiscation of peoples private information. (M5/72-80, 86)
	7. *[Industry$_4$]* Retrospective clinical research has been done at least a hundred years … always with what we refer to as presumed consent, which means that we send a protocol to an ethics committee and if they approve it then we do the research on the available data. (M5/250-3)	6. *[NGO$_2$]* Mixing the prospective and retrospective story is confusing ... deCODE has utilized a consensus that was given for a different set of issues ... and that is actually what's raising the problem. (M5/649-53)
Parliamentary approval	8. *[Parliamentary notes to the Icelandic bill:]* The disadvantage [of requiring informed consent] is that participation might be less, so that the database would be of less value. Clearly it would cost great effort, time and money to gain consent from every individual. (McGinnis 1999:2)	9. The Icelandic government's decision not to require informed consent because fewer people would be likely to participate, is unethical and unacceptable (McGinnis 1999: 6)
	10. *[Industry$_4$]* Not requiring informed consent for retrospective *[use of]* clinical data is the standard. Those of you who have not worked in medical science may be confused by some of the different sources of information, but … when the Icelandic parliament made that decision it was following what still is the international tradition. (M5/299, 317)	11. IC is the cornerstone of the ethics of medical research—it cannot be legislated by government [assent]. (McGinnis 1999:4)
	12. If it is incompatible with Western democracy to use information from medical records without informed consent, then there is no Western democracy. … The law of the HSD did nothing but endorse and put a legal frame around what is a common practice all over the world. (New England Journal of Medicine 2000: 2)	
Feasibility of IC		13. The scientific goals of the database could be just as easily obtained without violating the most basic ethical guidelines for investigations on humans. (Zoëga et al. 1999: 59)
Rules discussed	14. In epidemiological research the practice has been that consent need not be obtained for non-intrusive research as long as approval has been obtained from an ethics board. (ESHG 2000: 28/9)I	15. *HUGO Ethics Committee 1998:* archived samples can be used without consent [only] if they are anonymized. (ESHG 2000: 32)

Issue	Pro	Contra
	16. *British Royal College of Physicians (1999)* Secondary of human material samples does not require express consent of the individual. Requiring consent could bring all research on existing, archived material to a halt. (ESHG 2000: 28)	
	17. It would be prohibitively expensive to try to obtain a new consent from each donor for reuse of existing samples. (ESHG 2000:32, Reilly 1999)	
	18. *NBAC 1999*: Research on existing samples that are identifiable does not require informed consent and may receive IRB review, provided that it does not exceed minimal risk to the donor. (ESHG 2000: 29)	
	19. (*Icelandic Act on Biobanks 2000):* The board of the biobank may, if approved by the Data Protection Authority and the National Bioethics Committee authorize the use of biological samples for other purposes than those for which the samples were originally collected, provided that important interests are at stake, and that the potential benefit outweighs any potential inconvenience to the donor of the biological samples or other parties. (*Art. 9 paragraph 4)*	20. The Convention for the Protection of Human Rights (Oviedo 1997) requires IC for any future use of stored material (art 22). The treaty has not yet been signed by Germany, UK, B, Ireland. (ESHG 2000: 10)
	21. Centralized data base in Sweden contains health information about all patients released from hospital. In it information is retrieved without informed consent, without asking doctors and without opt-out provisions. (Milton 1999: 1)	22. In contrast to regulations governing disease registries the Icelandic database act does not simply legalize information collection, but allows combination with genealogy data and genetic data (Zoëga et al. 1999: 48)
		23. The sheer amount of data collected about individuals—for a reason that is different than its original purpose—calls for a variant of informed consent. While some database research could reasonably be performed with a presumed consent, studies involving linking to genealogy and genetic database should only be performed with an explicit consent from participants. (Zoëga et al. 1999:51)
Evolving standards		24. In Sweden and the UK extensive data collections have recently been announced by claims that the Icelandic model is to be avoided. (Mannvernd 1999: 2)
		25. Learning from mistakes Iceland made, the Estonian Genome Project requires that patients opt into the project after giving informed consent. (Estonia Genome Project 2001: 514)

Issue	Pro	Contra
Industrial policies		26. *[Industry1]* We have as a guiding principle first of all emphasized … the autonomy of the patient … we recognize an individuals right to self-determinism and privacy, of course; we respect these international and local standards, laws, cultural tenets. (M5/781-3)
		27. *[Industry3]*In establishing these databases and these collections of patient samples (whether we are doing it ourselves or through a third party) the company always obtains appropriate and explicit informed consent from patients that are enrolled in these kinds of studies in respect to both samples, tissue or blood samples and in respect to data that are taken for this analysis. (M7/577-81)
		28. It is the policy of GSK to obtain appropriate signed informed consents before *any* genetic research is conducted. (GSK 2001: 6)
		30. Samples are collected from consenting individuals enrolled in clinical trials conducted by Roche. The use of samples shall be restricted to the disease category and associated conditions studied in the clinical trial and/or to adverse effects encountered. (Roche 2001)

Proposed conclusion

In accordance with established professional practice and ethics exceptions from the requirement of IC should be granted for the use of anonymized health data and biological samples if such use is essential for relevant medical research and has been approved by appropriate review bodies.

Parliaments may have a mandate to extend such exceptions further and allow also identifiable data and samples to be used without IC. As a rule, however, identifiable data and sample should only be accessed with IC.

Researchers from companies should try to comply with this rule in all cases and seek IC for the use of identifiable data and samples even if exceptions from the principle of IC are legally conceded.

(2) General consent for unspecified genetic research

Question: Should general consent for unspecified genetic research in the future be admitted/asked for?

Main positions

Pro	Contra
• Competent individuals should have the right to give consent to broadly defined research in the future. The goal of the IC requirement is not to prevent research but to prevent research subjects from feeling cheated, powerless, misled or betrayed. **[Arguments 38, 40]**	• A blanket IC for unspecified genetic research projects in the future is in fact not *informed* consent. It should not be asked for if the data and samples are identifiable in those future studies and hence it is possible to approach the subject for specific re-consent. **[Arguments 33, 35]**
• Broad IC that would allow the use of data and samples for future, as yet unspecified projects, is not only an efficient and economical. It is also a legitimate approach, provided the research is approved by independent ethical oversight. **[Arguments 31, 34, 36, 41]**	• Given modern information technologies it seems possible and appropriate to seek specific re-consent for further research if the data and sample are identifiable (although they may be encrypted and the key only accessible by an independent third party). **[Argument 43]**

Arguments

Issue	Pro	Contra
Practical needs	31. [Industry$_4$]There is a scientific need to broaden the consent … if we could only do a consent on one specific disease and no more and if we wanted to study another disease or use that individual as a control for a different disease we would always have to go back and re-consent. (M5/577)	
	32. [Industry$_3$] Individual consent to a specific type of research and nothing else…that's not very practical. So we have been contemplating … a broad consent which would allow patients to decide if they want to participate in a research project that may involve not only the specific disease we are approaching them for but … any protocol subsequently approved by the national ethics board.(M5/278-88)	33. [NGO$_3$] A consent that could be made to any sort of research in the future…is not informed … it would be made without respect to information about the use of the consent. (M5/491, 4966)
Rules	34. A blanket informed consent that would allow use of a sample for genetic research in general, including future, as yet unspecified projects, appears to be the most efficient and economical approach, avoiding costly re-contact before each new research project. (ESHG 2000: 31, WHO 1998)	35. It is inappropriate to ask a subject to grant blanket consent for all future unspecified genetic research projects on any disease or in any area if these samples are identifiable in those subsequent studies. (American Society of Human Genetics 1996)

Issue	Pro	Contra
	36. Perhaps more than for other samples, it seems appropriate to ask a subject in the setting of a clinical biopsy or surgery to grant a blanket consent for future unspecified genetic research projects on the disease this person suffers from. (ESHG 2000: 32)	37. [Industry$_3$] Many people do want…a general [consent], for instance any neurological disease, any eye disease or even any disease… we should not take away the freedom of the individual to make those decisions if they want to … Freedom and self-determination should be the key to our approach to consent. (M5/293-9)
Patient/donor autonomy	38. Ethicists must recognize that research subjects, when well informed, have a right to participate even in broadly defined research. The goal of this approach is not to prevent research but to prevent research subjects from feeling cheated, powerless, misled or betrayed. (Greely 1998)	39. Informed consent in the strictest sense may not be possible for the database operation, however, a general consent requiring the operators of the database to outline the type of information entered, its potential use, and benefits and risks, seem a minimal requirement. (Zoëga et al. 1999: 47)
	40. It would be reasonable to give the individual the option to refuse permission for any secondary use … or permit any use without anonymization at the discretion of the investigator. (Zoëga et al. 1999: 29, Reilly 1999)	
Independent ethical oversight	41. [Industry$_3$] The approach which seems to be gaining some momentum is … ethical approval for such secondary use without specific informed consent through the use of some medical data panel, which I understand is a process operated in Denmark and which recently was favorably commented upon by the House of Lords in the UK. (M7/632-6)	
	42. [Industry$_1$]Ultimately that should trickle down into a moral mandate, namely to use this information for certain purposes and not for others….for those that benefit the individual and those that help it….to get better health care (M5/748-51)	
Industry perspective: Seek re-consent	43. For future epidemiological genetic databank initiatives, it may be possible to use de-identified samples/data…the code key held by a third party…[who is] able to identify participants [and can thus enable] specific informed consent for any future genetic research use to be sought. (GSK 2001: 5)	

Proposed conclusion

Research participants are entitled to full, specified information on the study to which they contribute data or samples. On the other hand, they have autonomy to be content with less than full information. They have the right to authorize that their contribu-

tions might be used in future, as yet unspecified research. Ethical rules require that such consent should not be accepted if the research entails unreasonable risk for the individual. Compliance with such rules must be guaranteed by independent ethical review of all research projects.

A different question is whether researchers, particularly from companies, should ask for broad consent and for how broad a consent. If data and samples have not been irreversibly anonymized specific re-consent of the research subjects might be feasible and should be considered if it does not imply unreasonable costs. Generally, it seems advisable, to circumscribe the type of diseases that could be studied in future research. Studies that can be expected to attract public concern, for instance in behavioral genetics or in the genetics of mental disorders, should only be performed with specific informed consent.

(3) Disclosure of possible social risks

Question: Should IC have to disclose the possible risks of genetic research for the society?

Main positions

Pro	Contra
• Subjects need to be informed about the risks of group discrimination that may be implied in the availability of genetic knowledge in the society. **[Argument 46]**	• There is a responsibility of researchers to oppose discrimination and exploitation not only in research but in the society. However, the goal of IC is to disclose possible risks for the individual research subject. Social risks that may result from the application of research must be regulated by the society. **[Arguments 47, 51]**

Arguments

Issue	Pro	Contra
Explaining the risks	45. The nature and the purpose of the data collection is very broad and it is difficult to predict the risks to the individual. Thus even if participants volunteer, they are not informed and comprehending. (McGinnis 1999: 6)	
Risks to society	46. Subjects need to be informed about the risks of group/individual discrimination that may be implied in the availability of genetic knowledge in the society. (Zoëga et al. 1999: 48)	47. [Industry$_5$] The creation of new knowledge should be regulated by [professional] ethical framework, the application to health care should be regulated by society [and not through IC]. (Stefansson 1999: 32)

Issue	Pro	Contra
Abuse of research	48. [NGO_4]Certain kind of data should not be analyzed below a certain level of aggregation, so that the possibility of individuals being put to risk is avoided institutionally (M6/243-52)	49. Data collected in the Roche Sample Repository shall only be analyzed in the aggregate. The RSR will not provide genotyping data on the level of individual anonymized patient records except to regulatory authorities and data monitoring safety committees carrying out interim analysis in the interests of patient safety. (Roche 2001: 2)
	50. The more information you collate, the more potential is there to abuse it. (Hodgson 1998: 1020)	51. [$Industry_1$] There is clearly a responsibility among our part as we engage in this research to oppose discrimination and exploitation not only in the course of our research but on the policy type level. (M5/783)

Proposed conclusion

The goal of IC is to protect the individual not the society. Individuals are free to deny consent if they consider the research as politically or socially risky or undesirable. But researchers can hardly be obliged to provide information needed for such decision. Criteria for what constitutes political or social risk are unclear. Protection against these risks must be provided by appropriate regulation. Researchers may have a responsibility to support such regulation. They must share the knowledge they have about possible impacts of the research on the society with regulators and the public.

(4) Disclosure of possible commercial use

Question: Should IC have to disclose the possible commercial use and value of the data and samples provided?

Main positions

- Potential research subjects should be told about the possible commercial value of the research and the possible embodiment of the work (or their tissues) as intellectual property.
- The informed consent form includes statements that subjects will not benefit financially from participation in the study, that the research results could have commercial and intellectual property value, and that the company will own the results of the research **[Arguments 52-55]**

Arguments

Right to know	52. Potential research subjects should be told about the possible commercial value of the research or the possible embodiment of the work (or their tissues) as intellectual property. (Greely 1998)
Scope of IC	53. [Industry3] [The company asks for:] 1. consent to undertake the research, which is specified in the patient consent form with an indication of what that might lead to; 2. consent to follow patent applications on any arising inventions and 3. to be able freely to commercially exploiting those inventions. (M7/581-5)
	54. The informed consent form includes statements that subjects will not benefit financially from participation in the study, that the research results could have commercial and intellectual property value, and that GSK will own the results of the research. (GSK 2001: 6)
	55. The subjects shall be informed that [they] will not be entitled to any financial gain from the participation in the study. [And it will be explained that] inventions, know how, and associated intellectual property originating from the use of [donated samples] shall become the intellectual property of Roche, except were agreed otherwise. (Roche 2001)

Proposed conclusion

IC forms must unambiguously point out that data or samples provided by research subjects will be used in projects that have a commercial perspective and that intellectual property rights will be sought by the researchers for results or materials derived from the projects. Only if IC is clear in this respect researchers can legitimately appeal to the willingness of subjects to provide access to data and samples as a gift.

(5) The right to withdraw the data

Question: Are there limits to the right of participants in medical research to withdraw samples and data?

Main positions

Pro	Contra
• The right to withdraw does not mean that all effects of participating in the research must be completely reversed. Material that has been produced from donated samples and results of studies already carried out can be kept. [Arguments 61,65]	• The patient who withdraws from the research has a right to withdraw all information about him/her from a data base to which he contributed during the research. [Arguments 56,58,60,61]
• Anonymized samples, immortalized cell lines, shared samples and samples used for research protocols cannot be withdrawn. [Argument 66]	• Research subject should have a right to withdraw data and samples that are identifiable (even if they are encrypted and the key only accessible by an independent third party). [Arguments 64]

Arguments

Issues	Pro	Contra
The principle		56. The Helsinki Declaration emphasizes that individuals are free to participate in research and that they can withdraw at any point without suffering negative consequences. (1.2: 41)
Arguments over the Icelandic HSD	57. Icelanders will be able to opt out at any time as well as during a period of more than six months following the passage of the database law bill, but before any data are actually transferred to the database. (Stefansson 1999: 30)	58. *[NGO$_1$]* In the health database there is no ability to withdraw … opt out at any time means that only new data will not be entered but the old data will stay … this is particularly acute in the case of children … when they become eighteen their data will still be in the database and so they had never had the chance to really get out of the database. (M5/633-41)
	59. One must not confuse the issue of being able to opt out of research performed with a planned research protocol and being able to opt out of a data base containing health information. Everyone follows the main rule that individuals can quit participation in research that they have agreed to participate in. (Milton 1999:1)	60. The position of the World Medical Association is that if a patient withdraws from scientific research, i.e., the data base, he/she should be able to withdraw all information about him/her from the research. (Milton 1999)
Future rules?	62. [This rule is] questionable if data are needed for research (public health) and encrypted—the data protection perspective of inalienable individual rights may not be in the best interest of the population's health. (ESHG 2000: 34 Nuffield 2000)	61. In most legislations individuals are considered to have an absolute right to give or withhold information about their genetic status and equally an absolute right to prevent their stored genetic data being transmitted. (ESHG 2000: 34)
Industry perspective	63. Control of the sample, including the right to withdraw while the associated clinical trial is in progress remains with the research participant. After that time the sample will be anonymized [more exactly: encrypted]and therefore can no longer be withdrawn. (Roche 2001: 2)	64. For future epidemiological genetic databank initiatives, it may be possible to use *de-identified* samples/data … provided to researchers in a double-coded format and the code key held by a third party … The third party [will enable] participants to withdraw at any time if they wished to do so. (GSK 2001: 5)
Limits of the right to withdraw	65. *[Icelandic Act on Biobanks 2000]* A donor of a biological sample can at any time withdraw his/her consent … and the biological sample shall then be destroyed. Material that has been produced from a biological sample by performance of a study or the results of studies already carried out shall, however, not be destroyed. (art. 7)	
	66. Anonymized samples, immortalized cell lines, shared samples and samples use for research protocols cannot be withdrawn. (ESHG 2000: 34)	

Proposed conclusion

Research subjects should have the right to withdraw their contribution (data or samples) at any time. This rule applies if the contribution is based upon free decision and not on legal duties. Withdrawal may become impossible or inappropriate if the data/samples are anonymized or shared with others or developed into secondary products. Such limits of the right to withdraw, or any other limit, should be disclosed in the IC form and specifically consented to.

(6) Community consent

Question: Should not only individual consent but also community consent be sought for the use of population data and samples in genetic research?

Main positions

Pro	Contra
• Doing human genetic research with populations from indigenous people presupposes not only individual informed consent, but also consent by the community. **[Arguments 69, 71, 72, 88]**	
• Human genetic research can have impacts on groups, for instance stigmatization or discrimination. It therefore requires a full group review and consultation and consent. **[Arguments 67, 76]**	• Group level protection against risks of genetic research must be provided through societal regulation and legislation. Group consent is not a meaningful requirement. Most "groups" that become involved in research have no organization or authority which can legitimately speak for the group. The indigenous communities are an exceptional case. **[Arguments 85, 88]**
	• Medical researchers should seek the support of advocacy groups of patients of the disease they study. And they should engage in a dialogue with the public to address concerns over genetic research. **[Arguments 87, 90, 91]**

Arguments

Issues	Arguments Pro	Industry Perspective
Principle	67. [NGO_5] Bio-prospecting that's going on in human genetic research … has impacts on groups and therefore requires a full group review and consultation and consent. (M6/38-41)	68. [$Industry_4$] We have to have two sets of responsibilities: responsibility toward the individual research subjects, … and responsibility towards the research community and ultimately towards society. (M5/222-6)

Issues	Arguments Pro	Industry Perspective
The case for CC: *Self-determination Nation/society as "community"*	69. [NGO_5] Each and every community has a right to make its own decisions about these questions. Basically that stems from a concept of sovereignty or self-determination…it's an inherent right and it's not one that can be conferred upon groups of people by somebody else. (M6/41-7, 58-9)	70. [$Industry_1$] We seem actually to be on the same plane…self-determination is nothing else than what I called societal consensus. As a society (and what in Iceland the population was discussing for a year and a half) we need to make a decision whether we want or do not want to do it and what and how. (M6/98-103)
Indigenous people as "community"	71. [NGO_6] As an individual, because I belong to a tribe, I don't have the right to give consent for my ancestry or for my future. (M6/168-73)	72. [$Industry_1$] If you go (as in the famous case for diabetes research) into an Indian population, it must be based on individual consent; it may very well, depending on the culture, be based on some sort of a community consent; I think that will vary from culture to culture. (M6/107-11)
		73. [$Industry_1$]We have as a guiding principle first of all …the autonomy of the patient….we recognize an individual's right to self-determination and privacy, and we respect these international and local standards, laws, cultural tenets. (M5/781-3)
Protection against group risks	74. [NGO_4] The Indian government decided not to pursue a bilateral project with a developed country regarding the immunological profile of Indian population because you could make the population vulnerable (in the event of germ warfare). … Surely we must debate and decide whether there are certain kind of data which we will not generate for certain populations, because that puts them at great risk in the current kind of society that we have. (M6/232-42)	75. [$Industry_4$]Clearly it's the right of any group or individuals to exclude themselves if they don't want to participate [in genetic research] … we had a discussion in Iceland whether we should exclude the psychiatric diseases because they were in some way more sensitive … it was quickly realized that if we left out that group of diseases we would be denying them the potential benefit (M6/280-90)
Patient groups as "community"	76. Because findings of DNA studies could lead to stigmatization, prejudice, and discrimination against the Icelandic people, the Icelandic people should be consulted before any research is done on a country wide scale. (Annas 2000: 1831)	77. [$Industry_1$] When we talk about biodiversity [in medical research], what we are actually talking about primarily is the diversity between health and illness … There has actually been very little population based genetic research so far … [in] the majority of the genetic research to date, the populations that it has focused on, are actually diseased populations. (M6/105-7, 114-5)
CC in the case of the Icelandic HSD?	78. [NGO_1] In this case the government has overstepped its legitimate powers. We see no pressing need in society that justifies this extraordinary database act. (M5/170)	79. [$Industry_4$] The Icelandic Health Sector Database Law was passed by a 2/3 majority in the parliament following 18 months of public and parliamentary debate … the democratic process comes together for a common decision. (M5/320-35)

Issues	Arguments Pro	Industry Perspective
	80. The democratic process was flawed. The outcome was determined a priori by the government. DeCode misuses the term "community consent". Icelanders were not asked whether they understand and [accept the details]. (Zoëga et al. 1999: 34/59)	81. [Industry$_4$] Twenty thousand people have opted out of the database … after three years of [campaigning by the critics].That is not a lot. Seven percent of the population in Iceland do not agree with what we are doing and have opted out … that is clearly their right and we respect that. (M5/336-41)
	82. [NGO$_5$] Iceland definitely at least was respected in the sense that they were consulted and made choices and decisions for themselves, whether or not those are good decisions. (M6/303-6)	
	83. [NGO$_6$] Roche's work is sensitive to the consent of Icelandic people….One must really commend Roche for due diligence, because [as far as I can see from the material] … they will use the information but the actual material will be left in Iceland; there is work done by Icelandic researchers, that to me says: they forward in the right direction. (M6/200; 221-6)	
Regulation as CC?	84. Action by the democratic parliament would be an indication of the community's willingness to participate (Annas 2000: 1831)	85. [Industry$_1$] [Industry] would actually welcome appropriate legislation … we want society to come up with rules how to use [genetic] information … we would, of course, like to participate when these guidelines are being decided upon. (M6/376-65)
Special procedures for CC?	86. ESHG 2000: If a population is to be the research subject, consent may be required at a group level (31). HGDP 1997: by the culturally appropriate authority.	
Support by patient groups as CC?		87. [Industry$_4$] There is no community that is more actively supportive of genetic research actually than these patient advocacy groups that exist for many of these diseases. (M6/115-9)
Regulation as substitute for CC?		88. [Industry$_1$] We need to protect individual research subject from direct harm…we need to ensure consent and protect their privacy…For the research community and society we need to conform to the rules, to the ethical standards. (M5/227-33)
Community consultation	89. Action by the democratic parliament which though desirable, is not necessary … rather what is required is a great deal of public discussion, so that all viewpoints an be aired and opposition can be expressed and addressed. (Annas 2000: 1831)	90. [Industry$_1$] We have the reality that people are concerned about genetics; there is this widespread fear which is perfectly understandable and quite legitimate and appropriate … along two lines: genetic manipulation [and] … dissemination of genetic information and the potential of misuse. (M5/ 724-30)

Issues	Arguments Pro	Industry Perspective
		91. [Industry$_1$] We as health care providers … [must] engage in a dialogue with the public … We want to do it in a neutral as possible fashion. It shouldn't be patronizing like it so often is when scientists talk to the common public. It must be a give and take. (M5/759-66)

Proposed conclusion

Genetic research with indigenous people should only be done with both the consent of the individual subjects and the consent of the competent authority of the community to which these subjects belong. The requirement of community consent reflects the fact that belonging to the community permeates all aspects of life for indigenous people.

Indigenous communities are a special case. Communities have a different meaning in the modern sectors of the societies. Typically, the populations or "groups" that become involved in research: patient groups, age groups, even ethnic groups are aggregates of people who do not constitute bodies that could legitimately speak for their members.

In modern societies the nation state can, of course, speak for all citizens. But under most legal constitutions nation states have to protect freedom of research, and they lack a mandate to decide whether individuals may or may not participate in a research project. Thus while parliamentary consent clearly reflects community consent it is not a prerequisite for legitimate access to individuals as subjects in research.

Community *consultation* is advisable to increase awareness of public concerns that may exist with respect to the research that is planned. Such consultation must be a genuine dialogue to be meaningful.

(7) In search of "best practice"

Arguments

Responsibility of industry acknowledged	92. [Industry$_1$] We as a company felt that it was very important to basically put on record how we think about genetics … what responsibility we have … in many ways just one facet of biology; but because of the sensitivities a somewhat special part of our research. (M5/777-80)
Efforts of industry acknowledged, need for a legal framework	93. [Expert$_2$] What some companies are doing is actually trying to preempt legislation in the field … to demonstrate that there is no need for legislation, but…there is a process of actually moving towards enhanced legislation because the capability of the research community to auto-regulate the issue has not been really proven to be sufficient. (M6/332-6)

How to provide legitimacy in drug development?	94. [Moderation] If you do it that way, will you will steer clear of problems of legitimacy … or what else could be done in order to make this a legitimate strategy for the development of drugs? (M5/840-3)
Anticipate appropriate legislation	95. [Industry$_1$] We are trying to preempt [anticipate] legislation, but actually in an effort to be conservative…we are trying to go the extra mile if you will but primarily because there is very little [regulation] that would provide us with the security that we seek...[industry] would actually welcome appropriate legislation … we want society to come up with rules how to use [genetic] information … we would, of course, like to participate when these guidelines are being decided upon. (M6/376-65)
Best practice for IC	96. [Industry$_3$] From our point of view we would take the position that it is important that the company complies with the best practice. (M7/588-9)

A2 Synthesis of Responses by the Participants

The principle of informed consent (IC) is unchallenged. Views differ, however, with respect to the regulations the principle implies. Industry tends to take a formal rule-of-law view that emphasizes the autonomy of the research subjects. Accordingly, it should be the choice of the subjects to say "yes" or "no" to the conditions of the research relationship, that is, whether or not to demand benefit sharing, allow data and samples to be stored after the research project has drawn to a close, give broad consent to future projects etc. (**R6: 1, 2, 5**). Stakeholders, in contrast, tend to take a substantive political view emphasizing the contexts of power relations and inequality in which research subjects take decisions. From their perspective, IC is not just the acknowledgment of autonomy, but foremost a mechanism that empowers the weak to resist the strong. Accordingly, no decisions should be accepted by which research subjects give away control or do not use options for control extensively ("aggressively") (**R6: 3, 4, 6**).

The difference may be more one of degree than of principle. Existing regulations do both: they acknowledge and strengthen subjective choice, and they impose some "objective" normative order that restrains choice. The Helsinki Declaration, for example, does not allow the research subject to give consent to unreasonable risk. On the other hand, autonomy is by definition politically ambiguous: it can be used to resist power, but also to give in. Perhaps one cannot remove this ambiguity completely without removing autonomy altogether. In any case, the specter of paternalism and elitism is around the corner.

The middle ground between the extremes leaves room for controversy. If one accepts that subjects can give consent to future research and/or anonymization of their data and samples, how broad could such consent be, and how should future uses of data and samples be authorized? Observers from industry insist that clear reliable rules be defined (including the role of review bodies) which "settle" the issues and at the same time preserve space for the pursuit of research (**R6: 2, 7**). Stakeholders seem to envisage an ongoing process of testing and renegotiating rules (and roles); they argue that in a precautionary perspective doubts over risks and rules should operate against the research (**R6: 4, 6**). Accordingly, the parties disagree over whether exceptions from IC requirements should be allowed and/or extended to population genetic

research and whether existing ethical review mechanisms are adequate safeguards (**R6: 4, 6**).

Informed Consent (IC)	Industry	Stakeholders/Experts
Principles	**R6: 2** What is needed are laws with clear-cut regulations that would not adversely affect research activities and would adopt safeguards to protect patient confidentiality.	**R6: 3, 4** Questions of IC must not be de-contextualized from relations of power and inequality, the link with BS must not be severed.
Exceptions from the rule of IC?	**R6: 2** In accordance with established professional practice and ethics, exceptions from the requirement of IC should also cover the possibility of proxy consent for patients who are unable to decide for themselves (children, unconscious people, mentally disabled people).	**R6: 4** A position of "no exceptions ever" might innocently foreclose a future benign opportunity. But the determination of exceptions must not be left to those who will benefit from them. **R6: 4** IC was in fact not given, if there was even the possibility of exceptions known to the researchers at the time that the IC was obtained. Under this logic, the positing of exceptions to IC in advance nullifies the entire IC process. **R6: 4** We need a kind of ethics version of the precautionary principle: the researchers need to demonstrate an adequate ethical schematic for their work in advance. Unless and until they do so, no exceptions should be permitted. **R6: 4** There should be no exceptions to the principle of no exceptions! **R6: 6** There is no wholesale or imperative "exemption" from the requirement of IC. Appropriately mandated ethics are permitted to waive the requirement in certain exceptional circumstances for a specific research protocol, if no more than minimal risks are implied for the subjects. **R6: 6** The risk of participating in genetic research exceeds minimal risk, because of the possibility of unexpected of results. Therefore, in general, waivers would not be expected in genetic research. **R6: 6** Parliaments do not have a mandate to exempt research from IC requirements.
Disclosure of risks to the society in IC		**R6: 3** A researcher, company or institution could direct people to websites that discuss such risks, so that it would constitute prior informed consent. **R6: 4** [Such risks must be disclosed]. No one can assert when, where and how unanticipated consequences of research mishaps will accrue, and to whom. Science, and science-based corporations [operate] in a matrix of societal, cultural and power relations.

Informed Consent (IC)	Industry	Stakeholders/Experts
		R6: 6 Researchers must disclose risks to the society they know of. **R6: 6** Results of genetic research can be both unexpected and predictive for others than the direct participant in a research project; therefore the risks involved will be significant for others, both family members and a more extended group.
Broad consent vs. need to re-consent	**R6: 2** Consent should not be limited to specific types of diseases, because then follow-up of coincidental research results with medical significance would be impossible.	**R6: 6** Consent means a voluntary agreement to a proposal or action and as such does not apply to something that is unknown or uncertain. **R6: 4** Under an ethical perspective, research subjects do not have a "right" to diminish the protection of privacy and the role of consent in research. IC does not occur in a mythical, de-contextualized world, but in a complicated world of uneven power and information [therefore, just referring to the autonomy of research subjects is inappropriate]. **R6: 6** The relationship between a corporation/researcher and a research volunteer is a mistrust-based relationship (unlike the trust-based patient-doctor relationship).Blanket "non-consent" opens up an avenue of "cheating" by the researcher [and is therefore inappropriate]. **R6: 4** [Broad consent] empowers the researchers who will directly and personally benefit from further research to take the relevant decisions; that eviscerates the ethics that could be established by the IC process.
Ethical review boards	**R6: 7** The need to have all research projects ethically reviewed [unduly] imposes more bureaucratic steps on genetic research.	**R6: 4** IRB review must not be used to replace the safeguards of IC—[it] cannot ameliorate the problem of allowing loopholes in the IC process. **R6: 4** Ethical review boards cannot adequately address the problems, as long as we populate our henhouse guardians with foxes.
Community consent	[Ethical review as community consent?]	**R6: 3** Indigenous communities should have the clear right to deny the use of their data or samples, especially if material was obtained previously without proper IC. **R6: 6** Community consent should be sought in addition to individual consent. **R6: 4** It is not apparent that non-indigenous people can have the state speak for them in ethical matters.

Informed Consent (IC)	Industry	Stakeholders/Experts
The right to withdraw data and samples	**R6: 7** The right to withdraw should not jeopardize research efforts if data are anonymized or intimately shared with others.	**R6: 4, 6** Research subjects can withdraw their data or samples at any time. No exemptions should be made for uses shared with others or for secondary products. Consented anonymization and publication are the only exceptions. **R6: 6** There should be assurances [monitored by IRBs] that remaining data and samples are destroyed when a research project is finished.

A3 Points to Be Considered for Conclusions

- Should any genetic research be admitted without IC? Apart from data and samples completely anonymized with consent? Should old collections of data and samples be available? Which body should review/authorize such research?
- To what extent can consent for future genetic research be granted? To what degree must the research be specified?
- How should risks to the society that might emerge from the results of genetic research be dealt with during the consent process?
- Disclosure of possible commercial uses and value of the data and samples.
- The right of participants to withdraw samples and data.
- Can *community consent* be interpreted as authorization by existing ethical review bodies? If not, which body has a mandate to give such consent? What is the middle ground between state control, on the one hand, and veto positions of a variety of mobilized groups, on the other?
- What are critical points in which companies could/should go “an extra mile”? What are the necessary steps?
- In view of the arguments discussed with regard to IC, can one think of elements of best practice that might be acceptable for both companies and stakeholders and could be taken up in some guidelines?

B. Benefit Sharing

B1 Survey of Arguments

Different types of benefits are at stake, and they accrue to different beneficiaries:

Benefits to individuals	Contributing to a public good, medical treatment, monetary payment
Benefits to community	Contributions to economic growth, to public health, and science; monetary payment
Benefits to humankind	Contributions to health and science

Benefits other than monetary payments seem to be less controversial. We therefore focus on arguments for and against granting **direct monetary benefits** to individuals and to the community.

(1) Monetary benefits to individuals

Question: Should direct monetary benefits go to individuals contributing to the research?

Main positions

Pro	Contra
• The fact that the research is done in a commercial context challenges the culture. Altruism is undermined. Patients increasingly consider data and samples as a commodity. **[Arguments 3, 5, 6, 8]**	• gift relationship prevails with patients contributing data and specimens to medical research. The patients want to contribute to a public good. The gift culture should be upheld. **[Arguments 2, 4, 7, 16]**
• If research subjects were fully informed about the commercial value of their contributions and the IPRs that will eventually be based on them, they might rethink their altruism. **[Arguments 8, 9]**	• The informed consent forms companies use to inform subjects about the research includes full disclosure of all commercial aspects of the planned research. **[Argument 10]**
• People who offer themselves as research subjects must not only be protected against risks; They must be treated fair; sharing the commercial benefits is a matter of fairness. **[Arguments 13, 14, 15]**	• Financial incentives are illegal. It is unethical. to "buy" consent to medical research. **[Arguments 1, 16]**

Arguments

Issue	Pro	Con	Other arguments
The principle of altruism		1. [Industry$_3$] In Europe it is illegal to provide any financial inducement to patients to provide samples and so no compensation is provided back to patients . . . consistent with the guidelines recommended by the MRC and that is the position that [our company] takes too. (M7/598-602)	
		2. [Industry] Patients are behind the company's efforts [to build a database] because consumers like the idea of participating in something historical, and the company is dealing directly with patients in the hopes of making scientific discoveries. (Philipkoski 2000)	
Altruism undermined?	3. [NGO] HSD makes the information on people's health records into a commodity as raw material for a business venture. (Arnason 1998: 2: 16)		
		4. The intention of donors is to further a collective good. (Greely 1997)	
???	5. [NGO] The assumption that samples and information are donated altruistically for the benefit of the greater good of the community is now being challenged. (Arnason 1998: 16)		
	6. [NGO] Increasing understanding among citizens that their genetic and health information is a valuable commodity. (Arnason 1998: 16)		
		7. [Industry$_3$] In English law it is unclear whether or not there can be any ownership of a patient sample . . . because of that uncertainty the MRC guidelines . . . recommend the adoption of a gift relationship . . . thereby if the patient has any rights of ownership they are transferred with those samples. (M7/591-8)	

Issue	Pro	Con	Other arguments
	8. It seems unlikely that the citizens of this welfare state would willingly make a large gift of their DNA to a for-profit US corporation. (Annas 2000: 1831)		
Informed consent to use for commercial purposes	9. Potential research subjects should be told about the possible commercial value of the research or the possible embodiment of the work (or their tissues) as intellectual property. A participant's altruistic feelings might well change on the extent to which someone else stands to profit from the research. (Greely 1998)		
		10. [$Industry_3$] The consent form used by the company includes consent to follow patent applications on any arising inventions and to be able freely to commercial exploitation of those inventions. (M7/581-5)	
BS in the Iceland case	11. [NGO_1] There is no effective mechanism of BS. The database cannot be used for the direct benefit of the patients that contribute data. (Zoëga et al. 1999: 56)		
		12. [$Industry_5$] Once risk genes are identified individual patients may benefit. (Stefansson 1999: 28)	
New rules?	13. Researchers must recognize that research subjects have interests beyond safety. (Greely 1998)		
	14. Great strides have been made to ensure that research is safe for human subjects, but thus far, too little attention has been paid to whether it is fair. On that question a social and legal consensus is lacking. (Greely 1998)		

Issue	Pro	Con	Other arguments
	15. A clear, generally accepted, and fair framework for the relationship with research subjects might impose some short term costs on researchers, but its absence is both dangerous to researchers and unfair to the people who offer themselves as human subjects. (Greely 1998)		
		16. [Industry$_4$] We do not want to create a culture where people sell biosamples and poor people would feel forced to contribute specimens. This would be unethical. (Response 1)	
		17. [Industry$_3$] From our point of view we would take the position that it is important that the company complies with the best practice. (M7/588-9)	

(2) Monetary benefits to the community

Question: Should direct monetary benefits go to the community in which the research is done?

Main positions

Pro	Contra
• Direct monetary benefits should be granted when the community makes special contributions to the research by providing additional infrastructure, as in the case of the Icelandic Health Data Base. **[Arguments 22, 23, 24]**	• The research will enhance economic prosperity, health and science: These are benefits justify the research, provided the benefits accrue in the community that participates in the research. **[Arguments 18, 19, 26, 27, 29]**
• The community should have a fair share of the commercial benefits if it contributes its DNA for the research. **[Argument 21]**	• The companies bear the economic risks of the research; they should be entitled to enjoy the profits *[within the general rules—taxes etc.]*. **[Argument 20]**

Arguments

Issue	Pro	Con	Other arguments
Indirect benefits are enough		18. The prospect of economic gain for the country and scientific knowledge that would lead to new drugs may be sufficient to justify research. (Annas 2000: 1831)	
		19. [Industry$_5$] The benefits accrue in terms of more efficient health care, high technology jobs. (Stefansson 1999: 30-1)	
		20. [Industry$_4$] The economic risk is taken by the researcher/company. The health and science benefit is indeed shared, so the question is only about the economic benefit. (Response 1)	
Advance agreement on BS	21. The community should have a realistic opportunity to benefit from the use of their DNA in research. It is critical that both the procedures for access and the financial aspects of the research venture are spelt out and agreed to in advance. (Annas 2000: 1831)		
BS agreements in the Iceland Case	22. Decode has to pay a big sum for the license. There is debate on whether or not this is a fair return. At least the principle is recognized that here is a national resource constructed by medical doctors and the staff of health clinics; and the people who made it should get something back—a fee and the annual fee for making profit from it. (Palsson 2000: 3)		
	23. Decode promises that Icelanders will get any drugs or diagnostics based on their genes for free during the patent period. (Enserink 1998)		

Issue	Pro	Con	Other arguments
BS agreements in the Iceland case	24. [Scientist from Cancer Society] The promise is a joke. How many drugs do you think are going to be developed and how many people will really benefit from it? (Enserink 1998)		
	25. The Icelandic government can make its own deal, but the deal would have been better had government bargained for a percentage ownership in the company (Annas 2000: 1831)		
Safeguards, rules			26. The Helsinki Declaration requires that the benefits of experiments with human subjects should accrue to the nation where they are done. It is unethical to do [clinical testing] in a poor country where it is known that the drug will never be used. (Milton 1999)
			27. [NGO_1] To ensure that benefits are returned to the community for whose collective good the sample was donated patient groups should be engaged… in UK: cancer patients kept control of intellectual property to ensure that benefits are returned back to that community. (Arnason n.d.:16)
			28. [$Industry_4$] Perhaps it is up to each community to decide how it wants to deal with potential future benefits and whether it demands a direct share in the economic benefits. (Response 1)

Issue	Pro	Con	Other arguments
			29. [Industry4] There may be a difference between communities where the research is performed by members of the community and those where outsiders are responsible for the research. Perhaps this is a part of community consent. (Response 1)

Questions posed to the participants

- Which arguments are missing in the above exchanges?
- Should one uphold the rule that no financial incentives be used to recruit people for participation in research projects?
- Has one to rethink BS if the community (the state) contributes to the infrastructure (database) used in the research?
- Should special rules apply when communities of indigenous people become involved in the research?

B2 Synthesis of Responses by the Participants

Questions of BS trigger responses in which the parties change sides, so to speak. Industry appeals to altruism, emphasizes a gift culture of not "buying" data and samples, and frames participation in research as cooperation for the production of a public good (even if that good will eventually be realized through commercial development) (**R2: 1, 4, 6**). In contrast, stakeholders emphasize the economic self-interest of donors; they accept the commodification of data and samples, and frame participation in research more as an investment into a commercial venture (**R2: 2, 3; R6: 3, 6**). A possible exception is admitted for clinical trials in drug testing (**R2: 3**).

While there seems to be consensus that (legal restraints notwithstanding) research subjects must be able to decide whether they wish BS or not (**R6: 7**), stakeholders require additional controls. Companies should not be allowed to seek informed consent for the use of data or samples without offering BS in the first place (**R6: 6, 3** vs. **R6: 7**). The research subjects may then choose to accept the offer or not. Such a scheme would make BS the expected rule and not gift giving.

Stakeholders thus proceed from the assumption that the research by companies means business, not science, and therefore research relations should be business-like (**R2: 3**). Research subjects may bargain for what they wish: upfront payments, profit sharing, or some control over IPRs derived from the use of data and samples (**R2: 3;**

R6: 6). Industry has the choice to decline the bargain if it considers the benefit claims out of proportion or an unacceptable restraint on its freedom to operate (**R2: 5**). Whether the business frame also applies for academic research where scientists seek personal gains through reputation needs to be discussed.

With respect to BS with the community, observers converge in that no special rules should apply for indigenous and other communities (**R2: 1, 3. 5, 6, 8**). But they apparently proceed from different assumptions—industry implying that BS with the community should not be required (outside clear CBD rules), and stakeholders implying that it should be required. This difference may reflect underlying disagreement over the legitimacy and justice of the profits made in (IP protected) drug development. Notwithstanding such disagreement, participants may want to consider that one rationale given (by industry) for not sharing the profits from commercial products is that the community gets indirect benefits through new drugs, new science and economic growth (**R2: 4**). This rationale fails, however, if the community from which data and samples are retrieved is not the community in which the commercial development and production takes place. (Along that reasoning the Declaration Helsinki strongly discourages clinical trials with populations that are not likely to benefit from the expected products.)

Benefit Sharing (BS)	Industry	Stakeholders/Experts
Trade or gift relationship?	**R2: 1, 4, 6** No financial incentives and BS should be involved for research subjects; "buying" consent and inducing trade in body parts must be avoided. A gift relationship should prevail with patients. **R2: 5** When the contribution of individuals is critical for the research plan, financial incentives may be appropriate. The rule should be that companies must have freedom to operate. **R2: 4, 6** Individuals benefit indirectly through better medical knowledge, health care and economic prosperity.	**R2: 2, 3** There is no rule in the U.S. that excludes financial incentives for subjects to participate in research. With BS, donors of HGRs will be more willing to participate, and relationships will become more transparent and business-like. **R6: 3** The concept of "gift" should not be assumed. If there is not an advance declaration of "reasonable" benefit sharing, individuals should not even discuss providing IC. **R2: 3** Participation in non-commercial research, in clinical trials for drug safety and in research where the participants will benefit from the results [may be appropriate without BS].
***Including BS in the* IC process**	**R6: 7** Researchers can legitimately appeal to the willingness of subjects to provide access to data and samples as a gift.	**R6: 6** Researchers should declare that they are prepared to share benefits and research volunteers, patient groups and society should aggressively negotiate share of IP and return of benefits. **R6: 3** In the case of a general consent to additional research, partners should agree to involve a third party to manage the increase in benefits if new outcomes are derived from the use of the data, including the licensing of patents or genes.
Fair amount of BS	**R2: 5** BS must be commensurate with the real contribution; individual body samples contribute very little; the companies bear the economic risk of the research.	**R2: 3** Upfront payments are better than profit sharing.

Benefit Sharing (BS)	Industry	Stakeholders/Experts
	R7: 8 Companies do not, as a rule, accept reach through claims on IPRs.	R2: 3 IPRs derived from the research should be considered in BS arrangements.
Use of databases provided by the public sector	**R2: 1** If the state is the custodian of samples and date, companies would expect to have to pay for access. BS is up to negotiations.	R2: 3 The State may decide to charge the amount a private company would have to pay if it had to seek access to data and samples without the public infrastructure.
	R2: 4, 6 Access to research infrastructure should be free; the public gets the benefits from the research. Compensation of costs may be appropriate, but not BS.	**R2: 2, 3** Some reimbursements of costs should be required; costs should be passed on for benefits the state hands to the private sector in the pre-commercial phase of research.
BS with communities	**R2: 4** No BS should be considered, research enhances economic prosperity, health and science, these are benefits. **R2: 5** BS with communities, too, must be commensurate with the contribution, e.g., authorizing individuals to participate in research. **R2: 9** Perhaps it is up to each community to decide whether it demands a direct share in the economic benefits from the research [for which data and samples are contributed].	**R2: 2, 8** Definition of community is unclear; benefits to the government may not be the right way—even not in Iceland. **R2: 8** Benefits should be assigned to the community even if it does not contribute DNA or additional infrastructure.
Special rules for BS with indigenous communities?	**R2: 1, 6** The same rules should apply to all peoples. R2: 5 Companies should follow state laws relating to indigenous communities. No specific rules except those in the CBD should apply.	**R2: 3, 8** Indigenous people should not receive more BS because they are indigenous. **R2: 2** There should be a set of rules respecting the culture of the indigenous communities. BS with indigenous communities should be separate from BS with the state.
Guidelines	**R2: 7** Developing countries and indigenous communities may lack parity in negotiating power; therefore, guidelines about what constitutes proper BS may be very useful. **R2: 7** Guidelines should consider what the developing countries themselves say that they want to do, not what some outside groups think these countries should do.	

B3 Points to Be Considered for Conclusions

- Is it realistic/desirable to expect that granting direct monetary benefits to research subjects becomes standard in research relationships? Also for academic research and in the social sciences?
- What are operational rules to define *BS with the community* in societies with a market economy? How would such BS fit the mandate of the state to regulate and tax the commercialization of new products?
- Given that the bargaining power of research subjects is weak and no objective measure is available to determine the economic value of their contribution to research, how can endless controversy over the adequacy of BS be avoided?
- Balancing the different aspects, which BS-points suggest themselves as guiding principles (or elements of a code) for corporate behavior?

C Research Consortia

C1 Survey of Arguments

We propose to focus further discussions of RCs on those aspects that are clearly related to the issue which is at the basis of the dialogue process, namely: What is the proper balance between the private and the public domain in dealing with genetic information?

RCs provide a model of how competition can be replaced with cooperation, and how research results which might otherwise be exclusively appropriated through secrecy or IP protection can be kept in the public domain. What are the prospects of this model? What are the limits?

Observers emphasize that RCs are feasible in areas of pre-competitive research. However, "pre-competitive" can hardly be defined in absolute terms. Genetic information that is regarded as pre-competitive by large drug developing companies (like those who participated in the SNP [single nucleotide polymorphisms] consortium) may be regarded as competitive by e.g. start-up firms who seek to commercialize any new information—provided they can reserve some exclusive right to its use.

Thus, it seems that institutional and legal frameworks play a role in defining or *constituting* certain areas of research as "pre-competitive". Accordingly, the arguments raised in the Working Group infer two types of reasons for considering research as pre-competitive:

- functional prerequisites of successful research that make strategies of private appropriation technically unfeasible,
- regulatory conditions that impose normative restrictions on the appropriation of research results.

Functional prerequisites	*The need to collaborate:* There are millions of SNPs; without collaboration nobody would ever figure out which are the 0.1 percent that are actually meaningful *[see argument no. 15]*
Regulatory conditions	*Rules of private-public partnership:* The Welcome Trust made a very substantial contribution to the SNP consortium under the condition that the data were going to be public domain. *[see argument no. 24]* *Limits on patents on genes:* The basic assumption of those who collaborated in the SNP consortium was that SNPs should no be patented. *[see argument no. 43]*

Conditions for successful RCs:

Question: Which are favorable/unfavorable conditions for the successful establishing of RCs?

Main points

Favorable Conditions	Unfavorable Conditions
• The SNP consortium demonstrates that RCs are suitable to keep genomic data in the public domain and limit patenting strategies that might block the further use of genes in research and commercial development. The model of the SNP consortium could be extended to further steps in genomic research. **[Arguments 1, 5, 36]**	• The SNP consortium worked because the research was clearly considered as pre-competitive by the companies that participated. This condition may not be fulfilled in research that investigates full length genomic structures. **[Arguments 25, 37, 39]**
• "Pre-competitive" is a relative term. Some companies may consider SNPs as competitive information and have an interest in patents that grant them exclusive rights over the commercial uses of SNPs. Hence, RCs can, apparently, be used to overrule company interests. **[Argument 27]**	• RCs must be compatible with the interests of the companies. They will only come about if companies define the research as sufficiently pre-competitive. **[Arguments 46, 48]**
• Interests can be influenced by institutional arrangements and public policy. Public financial contributions to genetic research may only be granted under the condition that companies do, in fact, define the respective genomic information as pre-competitive and agree to join a RC that places the information in the public domain. **[Argument 30]**	
• The dividing line drawn by patent laws between knowledge in the public and the private domain can be adapted. Genetic information that cannot be protected through patents is likely to be defined as pre-competitive. Accordingly, RCs in that area would be facilitated. **[Argument 49]**	

Arguments

The arguments cannot easily be framed into a pro/contra exchange. Many points raised in the working group were uncontroversial. The most interesting issues for further discussion seem to be whether RCs provide a model that can be extended beyond the SNP case to balance public and private domains in genomics and whether the viability of that model could/should be enhanced by appropriate modifications of patent laws. We collect the arguments according to the following scheme:

1. Functions/rules of RCs
2. Rationales for RCs: The case for public involvement
3. Rationales for RCs: Incentives for private companies
4. Preconditions for a RC
5. Examples of RCs (other than SNP)
6. Can the SNP consortium become a model for further collaboration in genomics?
7. Should legal frameworks (IP regimes) be adapted to facilitate RCs?

Functions/rules of RCs

Issues	Points raised
Keep genomic data in the public domain	1. [Expert$_1$] The key point is the decision to release the data continuously and not to keep them secret until publication. That leads to an enormous scale up in public domain. (M7/76-83)
	2. [Expert$_1$] Data from the SNP consortium are released to the companies and the public domain at the same time, that is one of the key point of the rules. (M9/909-21)
Defensive patenting	3. [Expert$_1$] All the data is freely accessible, and it is protected by submitting US patent applications to establish the data discovery. (M7/161-71)
	4. [Expert$_1$] The RC makes use of the patent system to guarantee that what was discovered remains in the public domain; it is a defensive patent. (M9/887,919)
Prevent patents that block the use of genes	5. [Expert$_1$] Gene patents are strong blocking rights, stronger than traditional patents, since they also inhibit other applications using the gene. With public-private RCs you eliminate some of these patents. (M7/347-60)
	6. [Expert$_1$] Since the data are placed in the public domain nobody can apply for a gene patent related to SNPs and restrict research. (M7/207-11)
	7. [Industry$_3$] The defensive patent can be activated as an invention registration; it gives you all the benefits of the date and serves to negate any subsequent patent application. (M9/924-7)
	8. [Expert$_1$] In the SNP consortium you can still get functional patents and a patent on a particular application. (M9/994-5)

Rationales for RC: The case for public involvement

Issues	Points raised
Public domain data as a prerequisite for research	9. [Expert$_1$] Collaboration and ownership contradict each other. The patent development and privatization of data resources inhibit worldwide collaboration; the RC is an alternative to make data more accessible (M7/60-7)
Prevent private data monopoly	10. [Expert$_1$] In the human genome project the public had to fight to keep the data in the public domain. It was only because the Welcome Trust doubled the same sum of money two days after CELERA announced its effort which drove the support of the NIH in preserving its funding. Otherwise there would have been a private data monopoly. (M7/90-101)
Suitable public infrastructures	11. [Expert$_1$]The computing systems at the Center provides an infrastructure for participation in the SNP consortium, and people are organized so that they can do a vast amount of research in a short time. (M7/388-94)
	12. [Expert$_1$] If you fund academic research properly you can produce large amounts of data and knowledge very effectively without needing to have the strong profit motive which is always quoted in the pharm[ceuticals] industry as the driving force. (M7/395-9)
Provide better access for researchers from poor countries	13. [Expert$_1$] By having the data in the public domain ion the RC you provide free access. If you have the data in the private domain, it does not matter how low the prize you charge for access, you are going to exclude a lot of researchers worldwide. (M7/376-9)

Rationales for RCs: Incentives for private companies

Issues	Points raised
Benefits from collaboration	14. [Expert$_2$] What is the motivation of companies to contribute to RCs and make data available even to those companies which do not contribute? (M7/404-6)
	15. [Industry$_1$] There are millions of SNPs; without collaboration nobody would ever figure out which are the 0.1 percent that are actually meaningful. (M7/427-30)
	16. [Expert$_1$] Companies are getting more out of the rest of the research: What would they loose by letting other companies see it? (M7/409-11)
	17. [Expert$_1$] As Allan Williamson (Merck) put it: You can only do a certain amount of research in your company; biology is just too complicated. For integrating all the information, the integration of different peoples' ideas and data becomes more and more critical. (M7/192-9)
	18. [Expert$_1$] Making data accessible becomes a centralized problem; if you are going to do research … potentially you require access to all this information regardless [of] whether you are a company. (M7/370-375)
	19. [Expert$_1$] If companies block access to private data, then they miss out on the analysis provided in the public domain. So, from their point of view it is worth giving the data into the public domain because of all the research they get back. That is the argument that these consortia [use]. (M7/199-204)
	20. [Expert$_1$] From the companies' points of view: the more free access there is, the more research gets done, [and] the more it benefits you on developing products. (M7/381-5)

Issues	Points raised
Failure of exclusive private strategy	21. [Expert$_1$] CELERA cannot report any genome from their data, but they can report from combining the public domain data and the private data. The whole genome job did not really work; CELERA was rescued by the fact that they could take a public domain mapped effort. (M7/112-3, 142-4)
Distributing risks	22. [Industry$_1$] The project was such that no company by themselves was going to take the high risk. (M7/433-4)
	23. [Industry$_2$] Companies which are solely motivated by profit … nevertheless frequently find research consortia to be the best way to proceed, typically when the research is pre-competitive and involves technology which would be too expensive for one party to develop. (M7/1105-15)
Complying with conditions for private-public partnership	24. [Industry$_1$] Welcome Trust made a very substantial contribution to the SNP consortium under the condition that the data were going to be public domain. (M7/421-2)

Preconditions for an RC

Issues	Points raised
Pre-competitive research	25. [Industry$_1$] The reason for companies to participate in the SNP consortium was the pre-competitive nature of the data. There was really no competitive pressure, and it was appreciated that unless you put the data in the public domain nothing was really going to come out of the research. (M7/421-34)
	26. [Industry$_2$] Companies frequently find research consortia to be the best way to proceed; but the conditions under which they find that to be true is that the research is pre-competitive. (M7/1110-14)
	27. [Industry$_3$] SNPs are pre-competitive for those who want to develop new drugs; our research tools are other people's products. It is always pre-competitive with respect to the members of the respective consortium. (M9/1022-39)
Limits to patents on genes	28. [Expert$_2$] The basic assumption of those who collaborated in the SNP consortium was that SNPs should no be patented. It would be a problem if SNPs could be patented in any country (M9/935-6)
	29. [Expert1] In the SNP consortium you can still get functional patents and a patent on a particular application .(M9/994-5)
Incentives through public contributions	30. [Industry$_1$] Welcome Trust made a very substantial contribution to the SNP consortium under the condition that the data were going to be public domain. (M7/421-2)
	31. [Expert$_1$] The computing systems we have at the center provide the infrastructure for the SNP consortium. (M7/388-94)

Examples of RCs (other than SNP)

Issues	Points raised
	32. [Industry$_2$] In two examples consortia generated [environmental] for the public; but when companies began to use the technology for themselves it became proprietary. The consortia ended and the participants patented the technology and applied it to individual commercial advantage. The public interest of having the right goods or the best services in the shortest time is generally met by a mixture of both public and private. (M7/1119-30).
	33. [Expert$_1$] There are plans that companies submit a list of structures that they are interested in determining; this list will be merged to remove redundancy, the attempt will be to get genomic coverage of structures. You apply for a patent to get the date on the structure and the data can be free available. (M7/185-91)
	34. [Industry$_1$] Harvard wants to put up a structural biology consortium (M7/435)

Can the SNP consortium become a model for further collaboration in genomics?

Issue	Pro	Con	Other arguments
Public domain data as a public policy goal	35. [Expert$_1$] Patents and privatization of data resources inhibit worldwide collaboration; the RC is an alternative to make data more accessible (M7/60-7)		
SNP RC as a model	36. [Expert$_1$] Having done the SNP consortium it is easier to present RC as a possibility for the future (M9/809)		
The limited value of the SNP model: pre-competitive research as a precondition		37. [Industry$_2$] The SNP consortium is an example that works: If the database were for full length gene sequences, it could be different. (M7/1130-36)	
		38. [Expert$_2$] All RCs so far, obviously, happened in the pre-competitive area. (M9/879-80)	
		39. [Industry$_1$] The pre-competitive nature of the data is the difference between the SNP consortium and a structural biology RC, or the FLEX consortium that Harvard wants to put up. When it comes to full length clones, the prospects for RCs are less clear. (M7/423-36)	

Issue	Pro	Con	Other arguments
Balancing private and public domains			40. [Expert$_1$] Not everything should be public property. But the use of infrastructures of research will be more efficient when you keep them in the public domain. (M7/1098-9)
Guidelines for establishing RCs			41. [Industry$_2$] One should define the characteristics when it is appropriate and why to collaborate in an RC. Guidelines and suggestions might be offered to different groups which find themselves in a comparable situation. (M9/800-5)

Should legal frameworks (IP regimes) be adapted to facilitate RCs?

Issue	Pro	Con	Other arguments
	42. [Expert$_2$] RCs require a legal environment; to provide this environment is a public policy issue. (M9/876-8)		
Preclude patenting SNPs	43. [Expert$_2$] The basic assumption of those who collaborated in the SNP consortium was that SNPs should no be patented. It would be a problem if SNPs could be patented in any country (M9/935-6)		
		44. [Industry$_1$] The consortium has a protection in US and in Europe, where it matters. If somebody patents SNPs in Nepal, let him do research there. (M9/961-3)	
Constitute pre-competitive information by limiting the availability of patents	45. [Expert$_2$] Define the dividing line between what should be patentable and what not. At which stage should patents come in, what information should be regarded as pre-competitive? (M19/971-5)		
		46. [Industry$_1$] If you can get the consortium together to work, then you have by definition an issue that is sufficiently pre-competitive to allow the RC. (M9/1000-2)	

Issue	Pro	Con	Other arguments
	47. [Industry$_3$] SNPs are pre-competitive for those who want to develop new drugs. Our research tools are other people's products. "Pre-competitive" is always defined with respect to the members of the respective consortium. (M9/1022-39)		
		48. [Industry$_1$] The definition of pre-competitive comes out of the prospective RC. (M9/1054)	
Demarcation of pre-competitive information as a public policy issue	49. [Expert$_2$] It is a public policy issue: If you do not have patent protection for certain kind of information RCs are much more likely, because there is no way to make it competitive information. (M9/1007-9)		
Limits of patents on genes	50. [Expert$_2$] The only way to have a RC working and avoid a situation where patents like the one on BRCA block research, is to exempt the gene from patenting. (M9/989-91)		
	51. [Expert$_2$] It is not in the public interest to have patents at the level below actual products … to have patents on genes when there is no product in sight. (M9/1033-5)		
		52. [Industry$_2$] Disagree that the research plan that enables you to patent a gene does not have a product in sight … a gene is halfway toward the ultimate product and may sometimes be the product. The [proposal to limit patents on genes] would be very difficult for us as a group to consider, but we could agree on something that is regarded as pre-competitive. (M9/1039-43, 48)	

Questions posed to the participants

- Is the argument that joint efforts of public and private research are necessary to cope with the complexities of genetic data valid beyond the gene sequencing project? Can it be applied to structural or functional genomic research?

- Is public-private partnership within RCs (which are public domain oriented) a viable strategy for the drug developing companies to establish the knowledge base for structural genetics, gene products, gene functions, and genetic factors associated with specific diseases?
- Would legal changes that restrict the options for patent protection of genetic information enlarge the opportunities for RCs? Under what conditions would such restrictions become a disincentive for drug development?
- Are these the wrong questions? Is any important argument missing?

C2 Synthesis of Responses by the Participants

The responses underline that the SNP consortium discussed in the working group must be distinguished from the usual types of joint ventures and public-private collaborations or networking (**R3: 1, 3, 5, 7**). Whereas the latter may aim at the development of a commercial product, including the establishment of exclusive rights on the results and allocating ownership of the data to the party that produced it, the former is explicitly designed to release useful information in the public domain (**R3: 6**).

The leading question in the 3rd Circular was, whether the SNP model could be extended to research further down the chain towards new products, e.g. to investigations of functional genetics and gene-disease associations–the implication being that the possibility to reserve exclusive rights would also be postponed to information further down that chain, e.g., to drug targets discovered on the basis of those investigations.

Stakeholders tend to argue in favor of such extension, not only for technical reasons (efficiency of research), but also as a policy principle that restricts the scope of exclusive rights granted for genetic information. The open source software is inferred as a model in this respect (**R3: 2, 4**). Representatives from industry have doubts. While not excluding such RCs altogether they anticipate incompatibility of interest, because the RCs would include knowledge considered as competitive (**R3: 1, 3, 5, 7**). The "business driver" for RCs is the pooling of costs and the sharing of risks in developing a knowledge base (**R3: 1, 7**). RCs are only viable if the interests of all parties can be met. For industry this would, as a rule, include the right to obtain patents (**R3: 1, 3**). Large companies may, however, also join RCs—and put the results in the public domain—to avoid that genetic information on which they will have to rely in the development of new products is patented by small start ups (**R3: 6**). If the results of RCs have to be placed in the public domain, companies must determine whether for them the benefits, e.g., in terms of public funding or freedom to operate, outweigh the price that they cannot claim exclusive rights on results and use these rights to protect and recover the investments in subsequent product development.

(Participants commented extensively on the question of whether restricting patents on genes would amount to a disincentive for drug development. These points are included in the next section on Gene Patents. The same applies for arguments that a proper balance between private and public knowledge can be achieved through existing mechanisms of patent law and that there is no need for "rebalancing".)

Research Consortia (RCs)	Industry	Stakeholders/Experts
Extending RCs to functional genetics?	**R3: 6** The argument that joint efforts of public and private research are necessary to cope with the complexities of genetic data is incorrect. Private research has all the means to cope with such complexities.	**R3: 2, 4** If RCs were seen as useful for sequencing efforts and mapping, by that token, they should be even more useful for structural or functional genomic research. RCs are creative forces and give back more than you put in.
Efficiency of RCs	**R3: 7** With so many genes whose function and structure await determination, pooling resources allows a higher volume of opportunities to be processed more quickly. If parties wish to collaborate in a research consortium, they should be free to do so. **R3: 3, 5** There are already a lot of RCs (contracts, joint ventures, networking between private and public institutions). **R3: 1** RCs can be fruitful and cost-effective ways to develop and share technology, but they can only succeed if all parties find the collaboration to be consistent with their long-term objectives.	
Results in the public domain?	**R3: 7** Whether or not patent rights are obtained in RCs, access to such rights is available by members and non-members, and results are put into the public domain, should be agreed upon by the parties.	
Competitive research	**R3: 1, 6** Functional genomics is a very competitive field. You are working with the utilities for genes and their associated expression proteins, which define the prime inventions in the area; and private entities would likely be very cautious in undertaking collaborations, which could greatly impact their right to develop and sell particular products. **R3: 7** The business driver for public and private partnerships relating to functional and structural genomics is not only the public/private domain issue but also the cost of the underlying work.	
Joint ventures—normal rules	**R3: 3** You need a win-win situation for the partners, i.e., incentives and costs are shared, including the possibility to obtain patents on the results. **R3: 6** Collaboration and ownership of data is not a contradiction. In pharma-public research collaborations ownership of data is usually allocated to the party that produced it, e.g., the public. Additional royalties can be offered in return for the grant of exclusive rights.	

Research Consortia (RCs)	Industry	Stakeholders/Experts
SNP consortium: exceptional case or post-competition culture?	**R3: 6** The SNP consortium is an exception to the classic collaborations, its objective being to release data in the public domain, which are pre-competitive and not patented. **R3: 6** The rationale for the SNP consortium was not just the desire to develop a research tool that will be publicly available and freely accessible to the entire scientific and medical community. It was also based on the need to create a commonly accepted SNP map more quickly, and with shared financial risk and less duplication of effort. **R3: 6** The primary goal pursued by private research through an RC that releases the genetic information in the public domain is to avoid patenting of the information by start-up biotech companies.	**R3: 4** One should not focus on pre-competitiveness as a condition of RCs, but draw an analogy with open-source software as an example of a post-competition culture. The resource is open to all, yet there are companies competing out there to sell this software.

C3 Points to Be Considered for Conclusions

- One question in the 3rd Circular was whether (public-domain oriented) RCs are feasible in functional genetics. Following the advice of an observer from industry we would like to ask *"the meeting parties for actual suggestions and test whether any consensus exists"* (**R3: 1**).
- Is public funding of RCs (and competition with private company efforts) an advisable strategy to bring public-domain oriented RCs together in functional genomics and research on gene-disease associations?
- Can one define elements of best practice for corporate strategies with regard to RCs?

D. Access to Databases

D1 Survey of Arguments

Health data bases and DNA sample collections are becoming important research tools in human genetics research. On the other hand, these tools are often private property. Even if the public sector contributes to the development of databases and sample collections, exclusive private rights may be granted for using them, as in the example of the Icelandic Health Sector Database (HSD) which has been exclusively licensed to deCODE by the government. The issue that emerges is the proper balance between

the private and public domain in regulating such tools/infrastructure for research. How should access to data and samples be granted?

Various questions arise in this respect:

- Should databases and sample collections be placed in the public domain because they comprise data and samples individual donors have contributed as a gift?
- Should they be in the public domain because/if they have been established with public support?
- What are proper conditions for licensing the use of the database? Should exclusive licenses be granted when access is sought for research with a commercial purpose? Should access be granted just for a fee? Is it proper policy to license the use of databases with reach-through provisions that allow the owner of the database to seize rights on results that will be achieved with the data?

Not all of these questions have been extensively covered by the participants of the dialogue process. We summarize some main arguments from our discussions and from the documents consulted. We confine ourselves to the issues of access to non-patented research tools. Questions relating to patentable research tools will be dealt with in the Section on *Gene Patenting.*

Should databases and sample collections for human genetics research be placed in the public domain?

Question: Should databases and sample collections for human genetics research be placed in the public domain, or, at least, be accessible with minimum restrictive conditions?

Main positions

Pro	Contra
• Data bases of health information and biological samples are crucial research tools for the advancement of medical knowledge. Unlike e.g. chemical libraries they build upon the personal involvement of large populations who contribute what they consider a gift for the collective good and not normally as a tradable commodity. Such databases should be accessible in the public domain to guarantee their maximum use for the collective good.	• Human subjects can legitimately transfer control of their data and samples to the owner of the database – including the right to use data and samples for commercial purposes. In fact, such transfer of control is often a precondition for mobilizing the investments needed to establish the database. Contributions to the collective good can still be expected: new products (diagnostics or therapeutics) will be derived from the commercial use of the database.
• In those cases where the public supports the database, through investment or special legislation, the database should be treated as a public infrastructure accessible in the public domain. Private investment could be compensated by the right to charge a fee for access, not by granting an exclusive license to use the data base.	• In a private-public partnership the private investment may only be available if exclusive rights to exploit the database are granted. Moreover, exclusive licenses may be needed in certain cases to provide incentives to use the database, e.g. in research on orphan diseases.

Pro	Contra
• Licenses for access to databases and sample collections should not impose undue restrictions of the investigators' freedom of research, such as reach-through provisions that give the licensing agent the right to claim the intellectual property of the results of the research.	• Licensing conditions should be left to the bargaining process between interested parties.
• Some companies have policy models under which they grant free access to their databases.	• The models apply for pre-competitive data, such as ESTs *(see Research Consortia)*. They are not viable for numerous small companies that specialize on the commercialization of the database as a product or service. These companies will try to protect their databases as trade secrets.

Arguments

Issue	Pro	Contra
Arguments over the Icelandic Health Sector Database (HSD)		
Violation of Freedom of Research?	1. The exclusive license for deCODE to exploit the data will stifle independent research and hinder freedom of inquiry and entrepreneurship. (Mannvernd 1999: 2)	2. [Industry$_4$] We are not imposing any new restrictions on the access by either academic or commercial scientists to hospital health data or genetic material. (M5/417)
	4. Icelandic investigators are concerned that patients will be in fact "locked in" to the licensee. (Mc Ginnis 1999: 6)	3. [Industry$_4$] The original data stays in the hospitals and may be accessed by physicians and scientists just as it has been for the last hundred years. (M5/324-7)
Monopoly?	5. It is disturbing that at a time when monopolies and special licenses are being done away in many fields this very ideology is introduced in biotechnology, one of the most important knowledge base of the future. (Erlendsson, Adviser to the Icelandic Prime Minister 1998)	6. The HSD will not exclude others from access to data from Icelandic patients nor give exclusive rights to develop new drugs. (McGinnis 1999: 5)
	7. [NGO$_7$] Giving one company exclusive rights on the database of a whole country is a little bit scary. (M5/478)	
Unequal access to a research tool?	8. The data base is an important [tool] for genetic research. The exclusive license creates inequity between scientists in Iceland regarding access to the database. (Zoëga et al 1999: 52/3)	9. Access to the database is free for the government and for academic researchers who agree not to hand over data to commercial clients. (1.1:30 deCODE)

Issue	Pro	Contra
	10. Access for scientists from collaborating institutions is negotiable for non-commercial purposes, but not legally binding; scientists outside collaboration must pay market prices for access. (Zoëga et al. 1999: 52)	11. [Industry$_4$] We have to make sure that access is sought for academic research and that it does not undermine our commercial use. (M5/390-3)
Non-exclusive access to health data	12. [NGO1] Contracts deCODE is making with the hospitals state that the access is only for the employees of the hospital and not for the academics not connected with the hospital (M7/456-8)	13. [Industry4] Employees of those hospitals will have free access to the database … [but] we will still grant access to, for example members of the university … it is stated in the contracts that it not excludes others. (M7/465-8)
		14. [Industry4] It would be ridiculous for us to try to block access to the HSD because when we build something and then not use it; … we could sort of sit on the central database. (M5/564-6)
Exclusive access to genetic data	15. [Industry$_4$] So other people can access that database. But what they discover does not get revealed until the exclusive rights holders [contractors] decides whether it is something they have the exclusive rights to know. (M7/501-3)	16. [Industry4] For the genetic data we have made an agreement with [company] for exclusive rights for the development of diagnostics and drugs … so to summarize: we have non-exclusive access for the database, and we are offering exclusive access for specific disease projects. (M7/468-70, 480-1)
		17. [Industry$_4$] The use of the database will be limited by the priority that comes from the contract with the [company] (M7/497-8)
Unequal opportunities to commercialize	18. The exclusive license to exploit the database for commercial purposes creates inequity between scientists in Iceland with respect to commercialization. Commercial funding is an important resource for doing genetic research. (Zoëga et al 1999 :52/53).	19. The exclusive right to commercialize the database is in exchange for bearing the costs for establishing and operating the database. The licensee is putting forth the capital to establish the database and is entitled to the benefits of the investment. (McGinnis 1999: 5)
	20. The exclusive license amounts to a monopoly on the collective property of a whole nation. (Enserink 1998)	21. [DeCODE] The exclusive license is an absolute necessity to make the project viable. (Enserink 1998)
		22. [Icelandic Research Council] The data base provides a rare opportunity for Iceland's researchers to become involved in some exciting science, which the government—whose annual research budget amounts to US $ 120 million—would never be able to afford. (Masood 1998: 1)
Should research infrastructures be kept in the public domain?	23. [Expert$_1$] Infrastructures for research should be kept in the public domain. (M7/1098-9)	24. [Icelandic government] While undoubtedly desirable, public sector investment in a data base is beyond [Iceland's] reach, and private sector finance is needed. Without the carrot of an exclusive license, no company would be willing to shoulder the required investment. (Masood 1998: 2)

Issue	Pro	Contra
Publicly funded collections or databases	25. [UK Medical Research Council] It is not appropriate for any one company to be given exclusive rights of access to collections of samples made with the benefit of public funds. (MRC 1999:6)	26. [Health Committee of the Althing:] The free access to the HSD for Icelandic academic scientists can be considered as a payment by the licensee for access to data from the respective health institutes and independent health workers. (Erlendsson 1998: 2)
		27. [UK Medical Research Council] Exclusive access to data derived from research using the samples is acceptable to give sufficient time to secure patent protection. (MRC 1999: 6)
Access for a fee	28. [UK Medical Research Council] Researchers may not sell for profit samples that they have collected with MRC funding. Recovery of reasonable costs, based on standard accounting systems is, however, acceptable. (MRC 1999: 5)	29. [Expert$_3$] [Even if] the contents of the database must not be subject to any protection by IPRs … what allows the owners of the database to ask for a fee is the added value, the fact that they compiled [it].… The result will be [some exclusivity]. (M7/1145-57)
Estionan scheme	30. [Estonian Genome Project] Ownership of raw data and samples resides with a non profit foundation formed together with the Health Ministry. Local academics get free or cheap access. The foundation creates a for profit company to commercialize the data under non-exclusive licenses. (Estonia Genome Project: 2001)	
Industrial policies	31. [Industry$_3$] We all have an interest in promoting medical research..[therefore the company makes] licenses generally available for using as research tools … to academic institutions on favorable terms; [and] … also to commercial organizations, but on certain competitive terms. (M7/637-42)	
	32. [Industry3] [The company] does not have a position… simply because we do not have a patient population database at the moment which is available for access … but my own personal view is that gene sequence databases are a research tool and therefore not different in principle to biological samples … and providing that the data sets are free from obligations to third parties, then one could make those available. (M7/643-51)	33. [Expert1] Some private companies tried to stop public investment in genome sequencing because they were going to do that. … The consequence [would have been] … a private data monopoly. (M7/90-101)
	34. [Industry2] I don't view my job as controlling other peoples' right to do research. [The company] freely granted research rights to the use of what some people think was a revolutionary research tool. (M9/172-181)	35. Some biotechnology companies license the use of their databases with restrictive reach-through provisions that give the company options to intellectual property rights considerably downstream of discoveries made by using the database. (NRC 1997)

Issue	Pro	Contra
	36. The NIH cautions investigators not to accept licenses with reach-through provisions which might impose unreasonable restraints on their work and restrict progress. (NRC 1997)	
	37. [Expert$_1$] The alternative approach to having companies do it privately and then sell it … is consortia, where companies get together and…all the data [and samples] gets collected in the public domain and is available to everyone. (M7/155-9)	

Questions posed to the participants

- Should special rules apply for the access to databases that have been established through private-public-partnerships?
- Should commercial research be treated different from academic research? Can access for academic and commercial purposes easily be distinguished?
- Should exclusive licenses for the use of databases be dismissed as a matter of principle to ensure maximum use of the research tool?
- Should one insist that licenses for database use must not be combined with reach-through provisions that seize downstream rights for what is done with the data? Is competition between databases the only way to prevent such practices?
- What are other pertinent questions/problems?

D2 Synthesis of Responses by the Participants

The leading question was whether special rules should apply if a DB was built with public support. Public support could either mean public spending, or authorizing the inclusion of data available in the public sector, or granting an exclusive license to build the database (creating a monopoly).

Observers from industry insist that the rules for access to the DB would have to be negotiated between the partners (**R7: 5**) and investments must be recognized in order to have the DB in the first place (**R7: 6**). These are obvious requirements. They apply regardless of whether the DB is built for commercial purposes or not. The same is true for the demand that the public partner should strive to secure effective sharing of benefits (profits) derived from commercial uses of the DB (**R7: 4**).

In contrast, other observers, both from industry and stakeholders, emphasize that access to DBs built with public support should be free and cheap (**R: 1, 7, 8**) The underlying rationale apparently is that such DBs must be considered (and operated)

as public infrastructure and not just as a commercial enterprise. Therefore, access rules must reflect the public function of the DB.

All observers find it difficult to distinguish between academic and commercial research. Some still advocate preferential rules of academic access to the DB on the basis of that distinction (**R7: 1, 3, 4**). Others reject such treatment as discriminatory and unfair competitive advantage for public scientists (**R7: 5, 8**). One observer acknowledges that commercial perspectives cannot be disregarded in academic science, but explicitly demands that the privileges of academic science should be extended to research with a commercial goal (**R: 7**).

Exclusive licenses to use the DB are treated as a purely technical matter by some participants from industry. Accordingly, such licenses are admitted if they allow efficient use of the DB (**R7: 1, 5, 6**). Others (including from industry as well) oppose exclusive licenses on grounds of public policy (**R7: 2, 5, 7, 8**).

Six of eight respondents are against reach-through provisions to compensate for access to the database. The reasons given oscillate between economic and public policy arguments (**R7: 1, 6, 8 vs. R7: 2, 3, 4, 5, 7**).

Access to Databases (DBs)	Industry	Stakeholders
Public-private partnerships ***Negotiated rules***	**R7: 5, 6** Rules and conditions will always be negotiated between the partners. Public or private, whoever puts together a database may or may not find it in his best interest to grant free access to his database. General rules must apply. **R7: 6** The rights of the party who invests effort and money in creating a database must be recognized. Otherwise, fewer databases would be created.	**R7: 2** Ownership of DBs should not lead to different treatment.
Special rules for DBs with public support	**R7: 1** If the partnership is funded by the public, then the public should have access to the data. **R7: 8** Applying the same rules as are applied for private databases would hinder the sharing of genetic knowledge because access costs would be prohibitive to the public sector.	**R7: 7** Databases established using contributions from public resources, such as the Icelandic database, should grant the same public access without strings.
Preferential treatment of academic research	**R7: 1** If possible, academic and commercial research should be treated different.	**R7: 4,3**Academic research often reaches the public domain without patent protection. Academic researchers must disclose their current or future, intended or potential corporate applications of the research. **R7: 7** To limit access to purely academic work stifles creativity by preventing academic scientists from exploring their ideas commercially.

Access to Databases (DBs)	Industry	Stakeholders
Same rules for academic and commercial research?	**R7: 5** Differential treatment of academic and commercial research would be discriminatory and counterproductive to the co-operation and networking between academic and industry researchers. **R7: 5** If Academic scientists are exempted by any access rules/costs, they would have an unfair competitive advantage.	**R7: 2** Research both for commercial and scientific purposes should be free from any restriction.
Exclusive licenses for using the DB? ***Public policy reasons***	**R7: 5, 8** Exclusive licenses could block or hamper new developments in medical research; exclusive use of public databases would be detrimental to the aim of the public sector to share knowledge and foster advancement of science. **R7: 5** A license-selling body/company would be ill-advised to grant exclusive licenses for tools which are needed by many teams in academia and industry—the body/company could be stuck with such licenses.	**R7: 7** Exclusive licenses and monopolies, as in the Icelandic case, have no role and should be dismissed as a matter of principle, to ensure maximum use of the research tool.
Economic reasons	**R7: 6** To prevent exclusive licenses would be counterproductive and would either lead to databases being created in secrecy or not at all.	
Reach-through provisions ***Public policy reasons***	**R7: 5** If you create knowledge out of these data, this is your own achievement and there is no reason for reach-through provisions. It should be in the natural interest of every licensee to make sure that no unacceptable and hindering restraints are imposed on his work. Competition is the best way to prevent it.	**R7: 7** A database should not get downstream rights for somebody else's creative use of the data. The database would then appropriate intellectual property from that person.
Economic reasons	**R7: 8** Industry usually does not use public or private databases imposing reach-through provisions. If public database holders pursue reach-through provisions they run the risk of losing all private users.	

D3 Points to Be Considered for Conclusions

- Should DBs established with public support be operated as public infrastructure, which means free and equal access (eventually for a fee)?
- DBs (whether private or public) are research tools. Should this aspect be considered in defining conditions for licensing the use of a database? Exclusive licenses? Benefit sharing? Reach through claims?

- What could be proposed as best practice for corporate handling of DBs in genetics? Both DBs owned by a company alone and DBs established through private-public partnerships?

E Patents on Genes

E1 Survey of Arguments

Patents on genes, and patents on parts of organisms or whole organisms, spark public controversy. The issues raised are heterogeneous. On the one hand there are moral arguments that the concepts and rules of intellectual property, as a matter of principle, should not be extended to living materials or living beings. The "No Patents on Life" postulate tries to capture these arguments. On the other hand, critics argue that the patents impose excessive restrictions on the access to (and the use of) the inventions of modern biotechnology. While the latter arguments also voice moral concerns about justice and fairness, they do not reject the very notion of patenting; rather, they challenge the scope of protection granted through patents. In particular it is held that some of the safeguards patent laws provide to secure a balance between private property and public interests, such as research exemptions and licensing mechanisms, are insufficient or do not work properly when it comes to patents on biological materials.

This circular will be brief in dealing with the moral debate over "No Patents on Life". (The issue was not discussed at any length in Montreux.) We will also only briefly touch upon the discussion we had over the proposal for a *Treaty on the Genetic Commons*. The main theme of this Circular is the problems of access to inventions and of the scope of patent protection.

With respect to the scope of patent protection a key question is whether product patents should be granted for genes (DNA sequences) under the same conditions under which they are granted for chemical molecules. Critics argue that such product patents offer too much for too little. The frame of reference for stating the "too much" is provided by societal functions, traditionally associated with and underlying the patent system, namely to compensate for investment in R & D. Accordingly, specific arguments raised are that product patents on biological materials imply undue restrictions of scientific research, and that they stifle innovation in the fields covered by the patents. We have used these arguments as *leading questions* in our survey.

Participants did not discuss the legal technicalities of the IP system for their own sake. A major concern was that developing countries might be put at a disadvantage through the operation of the system. We have collected these arguments under question 5. It goes without saying that the survey cannot be representative of the whole range of related North-South issues (e.g., national sovereignty over genetic resources). Nor does it imply any judgment as to the particular question of whether biological materials received from the South should be categorically kept free from any type of access-restricting IPRs in the North. Issues of IPR and access to medicines are surveyed in Circulars 5 and 8.

The merits of many arguments can only be assessed when the meaning and the conditions of patents on genes are clearly defined. While it is impossible (and perhaps

not the proper function of the dialogue process) to display all the technicalities of patent law, we have decided to summarize some (selective) propositions from legal documents and commentaries to illustrate *The Legal Framework for Patents on Genes*. These propositions are included in the *long version* of the argumentation only.

The architecture of this survey as follows:

A. The Legal Framework for Patents on Genes

B. Leading Questions:

1. Do patents on genes violate basic moral principles?
2. Should a policy be adopted that makes organisms and living matter in general, including genes, unpatentable and non-tradable goods?
3. Are patents on genes (or gene fragments/derived gene products) a barrier to research?
4. Are patents on genes blocking the development of innovative products?
5. Are patents on genes undermining the access of Developing Countries (DCs) to new technology?

The Legal Framework for Patents on Genes

Genes are patentable, although they are naturally occurring	US: DNA compounds having naturally occurring sequences are eligible for patenting when isolated from their natural state and purified, and when the application meets the statutory criteria for patentability. A patent on a gene covers the isolated and purified gene but does not cover the gene as it occurs in nature (USPTO: Utility Examination Guidelines, effective as of Jan. 5, 2001)
	EU: Biological material, which is isolated from its natural environment or produced by means of a technical process may be the subject of an invention even if it previously occurred in nature (EU: Directive 98/44/EC, Art. 3.2)
Sequence data alone is not patentable	US: The genetic sequence data represented by strings of the letters A,T,C and G alone is raw, fundamental sequence data, i.e., non-functional descriptive information (USPTO: Utility Examination Guidelines, effective as of Jan. 5, 2001) While descriptive sequence information alone is not patentable subject matter, a new and useful purified and isolated DNA compound described by the sequence is eligible for patenting, subject to satisfying the other criteria for patentability (USPTO: Utility Examination Guidelines, effective as of Jan. 5, 2001)
	EU: Whereas a mere DNA sequence without indication of a function does not contain any technical information and is therefore not a patentable invention (EU: Directive 98/44/EC, rec. 23)

Disclosure of the biological function of the gene as a necessary condition for "utility"/"industrial applicability"	US: (Use as a probe is not enough.) If a patent application discloses only nucleic acid molecular structures for a newly discovered gene, the claimed invention is not patentable. But when the inventor also discloses how to use the purified gene isolated from its natural state, the application satisfies the "utility" requirement (USPTO: Utility Examination Guidelines, effective as of Jan. 5, 2001) Specific utility … means the applicant has to know what the gene does. In the past, patenting of a gene sequence was allowed based on general claims such as using the sequence as a probe; now, such a claim would be insufficient (J. Grisham, 2000)
	EU: Whereas, in order to comply with the industrial application criterion it is necessary in cases where a sequence or partial sequence of a gene is used to produce a protein or part of a protein, to specify which protein or part of a protein is produced or what function it performs (EU: Directive 98/44/EC, rec. 24 The industrial application of a sequence or a partial sequence of a gene must be disclosed in the patent application (EU: Directive 98/44/EC, Art.5.3)
	US: (Not a substantial utility!) (Substantial utility) means that the sequence must have a real-world use, such as use as a diagnostic or a treatment for a disease. … It is not enough to make a general utility claim such as using the sequence to make a protein, without giving a real-world use for that protein. (J. Grisham, 2000)
Disclosure of the biological function of the gene as a necessary condition for "inventive step"/ "non-obviousness"	(Non-obviousness) The balance between costs and benefits should be taken into account in deciding the patentability of ESTs or SNPs or other research tools. This can be done under traditional law doctrines by, for example, finding "non-obviousness" less readily satisfied if the ultimate application of the information or tool is unknown (J. Barton, 2000)
Disclosure of the biological function of the gene in the patent application as a sufficient condition for "utility"/"industrial applicability"?	EU: "… whereas the industrial application of a sequence or partial sequence must be disclosed in the patent application as filed" (EU: Directive 98/44/EC, Rec.22)
	§1a III of the Draft German Bill stipulates that the criterion of industrial applicability of a gene or partial sequence of a gene be met by stating *in the patent application as filed* the *precise* function fulfilled by the claimed gene or partial sequence" Thereby the threshold of industrial applicability can be overcome, however, without any restrictions *per se* as to the scope which can be claimed. (Schrell, 2001)
	Apparently, the legislator starts out from the assumption that the subject matter is defined by the function and absolute product patent protection can be obtained for that matter as defined by said function. In principle, this objective is to be welcomed. However, the proposed implementation fails to take into account that the subject matter might not be necessarily fully defined by the disclosure of a function in the application, especially the description and sufficiently delineated against subject matter which is equal in structure but different in function. Only the disclosure of the function in the claims might entail any limiting effect as to the scope of the patent in the course of legal actions to be taken (Schrell, 2001)

Scope: Product patents on genes—When one utility is described, can all utilities be claimed?	US: The patentee is required to disclose only one utility, that is, teach others how to use the invention in at least one way. The patentee is not required to disclose all possible uses, but promoting the subsequent discovery of other uses is one of the benefits of the patent system. When patents for genes are treated the same as for other chemicals, progress is promoted because the original inventor has the possibility to recoup research costs, because others are motivated to invent around the original patent, and because a new chemical is made available as a basis for future research. Other inventors who develop new and non-obvious methods of using the patented compound have the opportunity to patent those methods. (USPTO: Utility Examination Guidelines, effective as of Jan. 5, 2001)
	EU: "… whereas, according to this Directive, the granting of a patent for inventions which concern such sequences or partial sequences should be subject of the same criteria of patentability as in all other areas of technology: utility, inventive step and industrial application, whereas the industrial application of a sequence or partial sequence must be disclosed in the patent application as filed". (EU: Directive 98/44/EC, Rec.22)
	If the inventive step as tested against prior art merely consists of the discovery of a function the applicant can be obliged at any stage in the application, interference or appellation procedure to amend his claims accordingly by disclosing the function of the claimed DNA sequence, i.e., to combine the sequence with the function associated, thereby restricting the scope of the patent. Third parties which make use of said DNA sequence for any purpose other than the one claimed don't violate the patent. But if the disclosure of the DNA sequence itself has to be seen as the decisive step, absolute product patent protection with all the ensuing issues of dependency is still fully justified, albeit such an unrestricted scope of protection might meanwhile only be granted in exceptional cases (J. Straus, 2001)
	"I also want to strongly emphasize that it is definitely desirable to limit the patent rights given to a well-defined and clearly proven useful function, since we know now that each single gene—of which we may have only 25000 to 40000 altogether in one human genome—may be involved in the production of a ten or twenty fold number of functional proteins, and many such proteins may be enmeshed in a number of different functions of an organisms' body. Assigning broadly defined patent rights to a specific gene plus its protein, for which only one function has been described, in such a way that all additional functions described in the future are also covered—even though common practice when receiving traditional patents on chemical or pharmaceutical substances—could be ruinous to an economic landscape of biotech start up's, because the actual inventor of a completely new marketable use would immediately be subjected to license-serfdom under someone else who did not contribute his own creative intellectual or practical efforts to that sort of new development. Sweeping genetic technology patents could thus sweep a promising new industry all too easily down to the drain." (Markl quoted in Straus, 2001)
Flexibilities of TRIPS	There is no obligation under the TRIPS Agreement to adopt an expansive concept of "invention", as is currently done by many developed countries. In particular, nothing in the Agreement obliges members to consider that substances existing in nature, biological or not, are patentable, even if isolated and claimed in purified form. (C. Correa, 2000)

(1) Violation of Basic Moral Principles?

Question: Do patents on genes violate basic moral principles?

Main positions

Pro	Contra
• Patents on genes constitute ownership of life, which is morally wrong. A patent involving human genes is an act that offends against human dignity. **(Arguments 1, 3, 5)**	• A patent gives no rights to use the invention. Holding a patent on human genes does not, therefore, amount to owning a human being or any part of him/her. To warrant the verdict of "offense to human dignity" there would have to be a societal consensus that patents on human genes are clearly inconceivable. No such consensus exists. **(Arguments 4, 6, 2)**
• Patents on genes devaluate living nature by reducing it to an industrial product. **(Argument 7)**	• While such devaluation may be morally offensive to some people, it is considered acceptable by many others in the society. Thus the objection falls into the pluralist realm of moral views in modern societies. As such it cannot demand general compliance. **(Argument 8)**

Arguments

Issue	Pro	Contra
Patenting of human genes as immoral act?	1. [Critics in EPO Relaxin:] Patenting human genes is intrinsically immoral. It violates Art 53(a) EPC which excludes patents "the exploitation of which would be contrary to morality" and EU Directive 98/44 which prohibits patents "the use of which offends against human dignity (recital 38).	2. Patenting human genes cannot be seen in line with what counts, for example in EU Directive 98/44, as violation of morality: patents on cloning of human beings, on modifying germ line genetic identity, on commercial uses of human embryos and on producing chimeras from human and animal cells (Art. 6 (2), recital 38).
Violation of human dignity?	3. [Expert$_2$] In a case before the European Patent Office critics argued that a patent involving human genes was an offence against human dignity, because it was some form of slavery. (M9/49-54)	4. To invoke the moral prohibitions under patent law one must "consider whether it is probable that the public in general would regard the invention as so abhorrent that the grant of patent rights would be inconceivable. If it is clear that this is the case, objections should be raised under Art 53 (a), otherwise not."(Goldbach et al.1997:79)

Issue	Pro	Contra
Ownership of life?	5. [NGO_3] Patents on genes amount to ownership of life, which has gone further down the road than it is comfortable for some members of the society and must be limited. (M7/1165-74)	6. [European Patent Office:] Patents covering DNA encoding a human gene do not confer their proprietors any rights whatever to individual human beings. No woman is affected in any way by the patent on relaxin—she is free to live her life as she wishes and has exactly the same right to self-determination as she had before the patent was granted (EPO Relaxin)
Devaluation of living nature?	7. Patents on life devaluate the living nature because they reduce it to an industrial product. (Greenpeace Germany, Press release 19-11-2000)	8. [Modern cultures accept that plant and animal life is in many respects treated as a product, as private property and as a commercial commodity in the society.]

Question posed to the participants

- What is implied in the argument that one should "acknowledge" (rather than merely "tolerate") that indeed for some people patents on genes are morally offensive?

(2) Should living matter be unpatentable?

Question: *Should a policy be adopted that makes organisms and living matter in general, including genes, unpatentable and non-tradable goods?*
(Refers only to the proposed Treaty on the Genetic Commons)

Main positions

Pro	Contra
• Under the terms of the *Treaty on the Genetic Commons* genes cannot be claimed as commercially and negotiable goods or intellectual property. The national rights (granted by the CBD) to control access to genetic resources shall, however, remain intact. **(Arguments 9, 11, 13)**	• The issues of commercialization and monopolization through intellectual property rights should be kept separate. The *Treaty* destroys the prospects of sharing the benefits from commercial uses of genetic resources. **(Arguments 10, 12, 16)**
• The *Treaty on the Genetic Commons* envisages for human genetics something similar to what the General Public License achieves in (open) software development: namely, to make genetic resources widely usable without commercializing them. **(Argument 15)**	• The proposal of the *Treaty* is at odds with recent trends in legislation which all condone patents on genes under certain conditions. (*See* **section A** *above*.)

Arguments

Issue	Pro	Contra
Proposed "Treaty on the Genetic Commons"	9. [NGO_3] The proposed Treaty on the Genetic Commons provides that "genes will not be allowed to be claimed as commercially and negotiable genetic information or intellectual property". (M7/701-3)	10. [$Expert_2$] The issues of commercialization and of monopolization through intellectual property rights should be kept separate. There may be a number of arguments to object to patenting pharmaceuticals, the commercialization aspect as such is not frightening. (M7/748-56)
Genetic commons and relation with CBD	11. [NGO_3] The Treaty on the Genetic Commons is not intended to extinguish the ability to insert control, what it does, it attacks the ability to commercialize. (M7/962-4)	12. [$Expert_2$] One should not return to the concept of the common heritage of [hu]mankind which basically gave companies the free right to use genetic resources. With the adoption of the CBD national sovereignty over genetic resources countries has been established (M7/1177-84)
	13. [NGO_8] The "Treaty on the Genetic Commons" rejects a sui generis regimes for access to genetic resources that seeks compensation in a commercial sense from these resources. It goes the route of less ownership, of anti-commercialization. (M7/902-4)	14. [$Expert_2$] With the adoption of the CBD and the establishment of national sovereignty over genetic resources countries have a right to claim benefit sharing for all benefits which resolve from the use of genetic resources. (M7/1177-84)
Open source software analogue	15. [NGO_8] The Treaty on the Genetic Commons proposes to have an analogue for human genetics to what the GPL (General Public License) is in software development. Nobody has ever commercialized a product developed under a GPL. (M7/951-3)	16. [$Industry_2$] Debates over patentability are frequent when you have a new technology where change is rapid and people are uncertain as to where that change will take you…I have heard this same discussion on three technologies: integrated circuits, software and now on biological materials … Rights in genes are fair and reasonable. (M9/147, 337)
Is gene patenting likely to prevail?		17. New areas of technology do not create the need for a whole new specialized patent law. In many ways the arguments used for DNA sequence technology resemble those voiced 30 to 40 years ago when polymer chemistry was an emerging technology. (Doll 1998:689)

Questions posed to the participants

- Given the fact that patent on genes have become a reality in the developed countries, should one not turn to the options and needs to have a better "fine-tuning" of the respective granting practices—in terms of standards of inventiveness and utility, scope of claims, research exemptions, licensing conditions?

- The International Treaty on Plant Genetic Resources for Food and Agriculture (formerly International Undertaking) provides that recipients of plant genetic

resources from the FAO-Multilateral System should not claim any intellectual property rights or other rights that limit the facilitated access to plant genetic resources for food and agriculture, or their genetic parts and components, in the form received. Should this approach be applicable to other subsets of biological diversity? From which sources?

(3) Are patents on genes a barrier to research?

Question: Are patents on genes (or gene fragments/derived gene products) a barrier to research?

Main positions

Pro	Contra
• Patents on genes grant broad claims that restrict the use of what are essentially research tools. Access to these tools, and hence the progress of science, is slowed down through the need to obtain multiple licenses and through the escalation of research costs from license fees. **(Arguments 18-20, 8-34)**	• The problems of broad claims can be handled within the patent law. The claims have already been considerably down-sized through stringent application of the existing standards of patentability. Some of the patents with broad claims may, in fact, be invalid. Moreover, research exemptions provide additional leverage to use patented inventions in subsequent (non-commercial) research. **(Arguments 21, 22, 23, 26)**
• Research institutes are not equipped to litigate invalid patents, and research exemptions are limited—in general they only allow one to work *on*, but not *with*, the patented invention. Therefore, licenses are still needed, and they often impose conditions (e.g. reach-throughs) that threaten the freedom of researchers to operate. **(Arguments 25, 27, 37, 43)**	• Patents on genes and license fees are appropriate. Without them small companies, who account for a large part of the dynamics of biotechnology research, would not be viable. On the other hand, no rational company would try to suppress or control academic research on the basis of a claim to a gene. Nor would it try to collect damages from an academic patent infringer. **(Arguments 33, 36, 38, 40)**

Arguments

Issue	Pro	Contra
Blocking research?	18. [Expert$_{11}$] Gene patents are quite strong blocking rights, much stronger than traditional patents. [The BRCA patent] inhibits not just applications for diagnosis, but a lot of other applications using this gene as well; so this gene is blocked. … Research groups developing new protocols … are getting letters from people claiming patent rights and saying they shouldn't be working on this. … The public is not getting access to new research because of these blocking rights. (M7/347-57)	

Issue	Pro	Contra
	19. [Expert$_2$] If one company identifies one specific function of a gene and gets the product patent for the gene as such [this] basically would require every other user of that gene, even if the gene shall be used for completely different purposes, to require a license from the original patent holder. (M9/104-14)	
Broad claims	20. Those who wish to introduce a new pharmaceutical product must negotiate an unwieldy number of licenses with firms that have patents on various steps in the research. … The problem is likely to become increasingly serious in biotechnology ... where the practical limit of claim breadth seems to be only the imagination of the claim drafter. (Barton 2000: 1933)	
Rules restricting broad claims		21. [The scope of patents on DNA sequences is being restricted] The granting of comprehensive claims to downstream DNA products such as full length genes or to ultimate proteins is unlikely in the absence of a significant amount of information about the gene and protein being disclosed in the patent application. (Doll 1998:690)
		22. [Patent offices of Europe, Japan and the U.S.] Regardless of whether the specific function (e.g., the relationship to a specific disease) of a receptor protein is disclosed, the claims for agonists (active compounds) in general identified by the said screening methods … do not meet enablement and/or support requirements, considering the general scope of the claims. (Trilateral Project 2001: 18)
The defense of invalidity	24. Under the current USPTO reexamination less than a quarter of the patents reexamined survive without change. (Barton 2000:1934). Only recently, several patents filed in the eighties on TAQ-polymerase (an essential research tool with PCR) have been found to be invalid in the US and Europe (Nature Biotechnology 2001: 607)	23. [Patents on research tools that claim a broad range of research activities may be vulnerable to litigation.] They are more likely to be invalid for insufficient disclosure because the original specification [at the time the patent application was filed] was not directed at that activity and may not have been contemplated it. (Gogoris/Ancona 2001: 1076)
	25. [Researchers, especially from academia, may not be able to litigate the patent. Therefore, even invalid patents can have blocking impacts.] Current [U.S.] law creates a statutory presumption that strongly favors the holder of even an invalid patent. (Barton 2000: 1934)	

Issue	Pro	Contra
The defense of research exemptions	27. Research exemptions are quite limited. German Patent Law grants the exemption only for research for testing purposes" (Art 11, no. 2). This would, according to established court rules, include the search for novel functions and applications of the protected genes. It would not, however, include the use of the gene as a tool for research that is work with rather than on the invention.	26. [Industry$_2$] There are things like research exemptions and compulsory licenses on working requirements, [so] even if we [as a company] were uncooperative, people would have research access to our patented technology. (M9/337-45)
Relevance of the problem	28. Difficulties [are] created when research on complex systems is restricted by a thicket of patents on individual components of the systems. (NIH 1997-1:7)	
	29. [Merck] Problems can arise when access to related components of biological systems is blocked. For example, … a rational approach to discovery of improved schizophrenia drugs would be to target specific dopamine receptors. But if different companies hold patents on different receptors, the first path to an important and much needed therapeutic advance can be blocked. (NIH 1997-1:7)	
	30. Research on a complex system, for example receptor biology … [may] require obtaining multiple licenses on individual components of the system. (NIH 1997-1:7)	
	31. Proteins and even parts of proteins, characteristic arrangements of molecules (motifs), folds and subsections are already subject to the same welter of patent claim and counter-claim as DNA sequences. (Bobrow/Thomas 2001: 763)	
	32. [Bristol-Myers] The biomedical community has not yet truly grappled with the possibility that a large number of genes could be controlled by the rights of a relatively small number of parties (NIH 1997-1:12)	33. [Small biotechnology companies need patents to mobilize venture capital] There are upwards of 2,000 biotechnology companies in the United States; they represent a market capitalization of 60 billion [US dollars], of which 46-7 billion a year is spent on research. (NIH 1997-1:6)
The need to negotiate multiple licenses	34. Patents on materials … are essential research tools … e.g., receptors needed to screen drug candidates. … Because much research requires a multiplicity of such research tools, the stacking of royalties required greatly escalates research costs. (Murashige, 2000)	

Issue	Pro	Contra
The availability of licenses	35. To learn as much as possible about the therapeutic effects and side effects of potential products at the pre-clinical stages, [researchers] want to screen products against all known members of relevant receptor families. But if these receptors are patented and controlled by different owners, gathering the necessary licenses may be difficult or impossible (Heller/Eisenberg 2000: 699)	36. [Industry$_2$] I don't view my job as controlling other people's right to do research. [Our company] freely grants research rights to the use of what some people think was a revolutionary research tool, the gene gun. … In fact it's unethical for me as an attorney to imply that they don't have the right to use the gene gun. (M9/171-86)
Practices of companies holding patents on research tools	37. Cetus Corporation initially offered the scientific community to license PRC under a reach-through agreement to pay royalties on all second-generation products derived through research with PCR (NIH 1997-1:4)	38. Human Genome Sciences: "We would not block anyone in the academic world from using [the CCR5 receptor] for research purposes". But if anyone wants to use the receptor to create a drug, HGS will enforce its claim. (Hollon 2000)
	39. [Merck] We placed the Carrageen footpad assays in the public domain, and many companies used them to develop new drugs. Today, Merck would patent such an assay and use its patent to trade with other companies for access to other research tools. (NIH 1997-1: 7)	40. Any attempt to suppress research on the basis of a claim to the gene itself is bound to attract opposition from a number of research groups and not solely in academia or hospitals. (Crespi 2001:10)
		41. [Bristol-Myers] We all know that it is not good form to sue researchers in academic institutions and stifle their progress. Consequently, much potential litigation has been held in check. … I hope that this rational forbearance will continue. (NIH 1997-2:5)
		42. Damages in the case of patent infringement generally cannot be collected from an infringer who is merely engaging in research. (NIH 1997-2:5)
	43. For-profit organizations must minimize the encumbrances they seek to impose upon not-for-profit organizations for the academic use of their tools. Reach-through royalties or product rights, unreasonable restraints on publication and academic freedom, and improper valuation of the tools impede the scientific progress whether imposed by a not-for-profit or for-profit provider of research tools. (NIH 1999)	

Questions posed to the participants

- Should the experimental use (research) exemptions be extended by adopting a kind of "fair use doctrine" that gives free access to patented matters for research purposes (except perhaps when the research tool is provided as a marketable product, e.g., an instrument or a test kit)?
- Can "fair use" granted for research purposes be reliably distinguished from use for commercial development?
- The impact of gene patents on the dynamics of biological research may be ambiguous. Blocked access to research tools can operate as a barrier for some research institutes. On the other hand, small biotechnology companies that develop such tools depend on intellectual property protection to raise the venture capital for their work. These companies contribute considerably to the dynamics of research. Should one treat this tension as a question of efficiency (resource allocation) or as a question of public policy principles (proper balance of private and public knowledge and research)?

(4) Are patents on genes blocking innovation?

Question: Are patents on genes blocking the development of innovative products?

Main positions

Pro	Contra
• Patents on genes create monopolies for inventions to be used early in the R & D path towards useful products. They grant the patent holder rights to veto (or to charge license fees for) a vast number of potential downstream products, including applications that were not known when the patent was filed. These rights block the efficient translation of the invention into products. **(Arguments 50, 52, 54, 58, 59)**	• The monopolies granted by patents are the proper price society pays for the incentives for invention and disclosure. The dynamics of biotechnology research seem to suggest that the patent system functions and patents on genes do not pose great problems. New inventive applications of a patented invention can be protected by secondary patents **(Arguments 51, 53, 57)**
• Secondary patents are dependent. A license for using the first invention is still needed. With patents on genes any useful product is likely to cross the boundaries of several patents. Royalty stacking and reach-through licenses threaten to make the development of new products economically unfeasible. **(Arguments 55, 58, 60)**	• Companies can retain freedom to operate through cross-licensing negotiations. Reach-through agreements are not *per se* inequitable. They are a means to relate the value of the patented invention to market values; this method is also applied in benefit-sharing arrangements under the CBD. **(Arguments 56, 61, 62, 63)**

Arguments

Issues	Pro	Contra
	44. [Expert$_1$]It is not in the public interest to have patents at the level below actual products; … [when you] have patents on genes there is no product in sight. (M9/1033-5; no. 994)	45. [Bristol-Myers] If the gene was secured only after years of investigation. … Directors of corporate research ... would have to think hard before recommending a course of action that could result in widespread availability of that target in the community at large. (NIH 1997-2:4)
	47. The patenting system should help people channel their energy towards inventions of genuine therapeutic or diagnostic value and discourage frenetic cataloguing DNA sequences that are a long way from being a final useful product. (Bobrow/Thomas 2001: 763)	46. [Industry$_2$] [We] disagree that the research plan that enables you to patent a gene does not have a product in sight. … A gene is halfway toward the ultimate product. (M9/1039-43, 48)
Broad claims	48. [NGO$_1$] Unlike chemicals genes have variation. If you have a variant, you will get a protein that behaves totally differently and [the use of that difference] is prevented by that patent. (M9/420-2; no. 942)	49. [Industry$_3$] Agreement between us in terms of the undue breadth of claims that are granted … given the existence of a patentable invention. …The scope of the claim should be commensurate with a step forward in the art that the invention represents. (M9/562-7)
Patents on genes create monopolies	50. [Expert$_1$]Gene patents are quite strong blocking rights, much stronger than traditional patents. [The BRCA patent] inhibits not just applications for diagnosis, but a lot of other applications using this gene as well. (M7/347-57)	51. In any well-functioning patent system, by conferring monopolies in discoveries, patents necessarily increase prices and restrict use—a cost society pays to motivate invention and disclosure. (Heller/Eisenberg 1998:699)
	52. [Merck] Patents have slowed the progress of PCR products from the research laboratory to the marketplace. … Highly sensitive diagnostic tests for HIV RNA are too expensive for wide-spread use, largely because of the licensing fees charged by Roche. (NIH 1997-1:4)	53. Once a product is patented, that patent extends to any use, even those that have not been disclosed in the patent. [However] a future non-obvious method of using that product may be patentable … [the inventor] is not prevented from obtaining the second patent. (Doll 1998: 690)
	54. [Merck] A rational approach to discovery of improved schizophrenia drugs would be to target specific dopamine receptors. But if different companies hold patents on different receptors, the first path to an important and much needed therapeutic advance can be blocked. (NIH-1:7)	
	55. If gene sequences are treated as separate “inventions”, any useful product is highly likely to cross the boundaries of several patents. (Bobrow/Thomas 2001:763)	56. [Industry$_2$] Agree that even for a [big] company freedom to operate questions are very complex today. … [However] rights in genes are fair and reasonable and the techniques that exist including the patentability of second indications … have been shown to provide enough basis for [resolving the issues around] the uses of genes, because of the leverage for cross-licensing situations, so we haven‘t had a problem yet. (M9/158; 348)

Issues	Pro	Contra
Royalty stacking	58. When research on a complex system, for example receptor biology …, requires obtaining multiple licenses on individual components of the system, [the need] to pay substantial royalty fees on any useful application derived from that product … can swamp the development costs of some therapies to the point where development is not economically feasible. (NIH 1997-1:7)	57. Just as the issuing of broad claims at the early stages of [polymer] technology did not deter development of [new] polymers, the issuing of broad claims on genomic technology should not deter invention in genomics. (Doll 1998:689)
Reach through license agreements	59. The license for the use of its patented onco-mouse gives DuPont the right to participate in future negotiations to develop commercial products that fall outside the scope of their patent claims. The license terms permit DuPont to leverage its proprietary position in upstream research tools into a broad veto right over downstream research and product development. (Heller/Eisenberg 1998:699)	
	60. Reach-through license agreements appear to become more prevalent. In practice, they may lead to [a blocking situation] as upstream owners stack overlapping and inconsistent claims on potential downstream products. (Heller/Eisenberg 1998: 699)	61. Reach-through licensing creates a license the value of which can be measured. The value of basic research is usually not known. Thus, reach-through licensing may be necessary to compensate for the use of a [patented] basic research invention. (Kowalski/Smolizza 2000)
		62. For-profit companies have offered minuscule lump sum execution fees that would barely cover the prosecution costs for patent protection for basic research, only to agree eventually to proper annual payments and royalties based on a percentage. (Kowalski/Smolizza 2000)
Reach trough in benefit sharing for genetic resources		63. To demand reach-through royalties cannot be per se considered as inequitable. Reach-through royalties may be a proper way of compensating the contributing of enabling technologies or genetic resources without which the end product would not have been viable. (Cf. also Circular 2 on Benefit Sharing)]

Questions posed to the participants

- Is there a difference regarding the dependence of possible downstream inventions between patenting (and using) a gene/receptor and patenting (and using) building blocks of basic polymers?
- Is there any empirical test to determine whether patents on genes do on balance operate as a barrier to the development of useful products from discoveries in genetics?
- Is a tightening (strict observation) of the patentability standards sufficient to avert problems of too many dependency licenses in the development of new products?
- Should the scope of product patent protection on DNA sequences be limited to certain specific functions which would have to be precisely stated and disclosed?
- Would specific use and process claims (without granting any product patent protection) suffice to protect legitimate interests—given the mandatory TRIPS stipulation that process claims automatically extend to the product directly obtained?
- Should guidelines be developed to distinguish and provide transparency of best practices deployed by companies whenever they make use of their legally granted patents on genes?

(5) Patents on genes and developing countries

Question: Are patents on genes undermining the access of Developing Countries (DC) to new technology?

Main positions

Pro	Contra
• To cope successfully with the intricacies and ramifications of the international patent system, especially to litigate dubious patents, is beyond the legal and economic capacities of most developing countries. **(Arguments 67, 77, 79, 80)**	• To enforce patents through litigation is difficult and costly. Therefore, companies prefer to cooperate whenever possible, e.g. by licensing their research results out on reasonable and favorable terms. So there is ample room for the design of case-specific agreements that serve both the partners from DCs and the holders of the patents. **(Arguments 73, 76, 88, 89)**
• Patents on genes in combination with restrictive licensing practices will undermine the technology transfer objectives of relevant international agreements such as the CBD and bar access to new and competitive technology. **(Arguments 64, 82, 83, 86)**	• There are explicit commitments (e.g. in the CBD) to facilitate access of DCs to relevant technologies using germplasm. These commitments can be expected to have impact. They are not only designed to benefit government agencies in DCs but private companies in the South as well. **(Arguments 84, 85, 87, 90)**

Arguments

Issues	Pro	Contra
Scope of the problem	64. We need to find out whether current IP practices present a barrier of access to platform and enabling technologies that are most useful for developing countries. (Barton/Straus 2000)	65. [Industry$_3$] There are actually very few patents granted to companies from the North in poor Southern countries. (M9/657-61)
	67. [NGO$_8$] We are moving towards a globalized economy with global implementation of patent law. Patent offices in Southern countries have not the capacity and cannot be expected to evaluate and litigate claims. (M9/623-30)	66. [Industry$_2$] We cannot afford the effort to file in countries where we don't do business and where we don't have an interest. (M9/657-61)
Territoriality of patents	68. [Industry$_2$] Greenpeace claims that the issuance of a patent in Europe will prevent indigenous farmers from using existing materials in Mexico. (M9/282-93)	69. [Industry$_2$] There is no extraterritorial enforcement of patent properties. And if indeed the six varieties that were mentioned as existing in Mexico have the characteristics of the varieties that [company] is claiming then the patent will not be granted. So indigenous farmers in Mexico have nothing to worry about. (M9/282-93)
Misperceptions of patent law	70. [Expert$_2$] Even the international agricultural research system is under this misperception that they have to comply as an international institution with patents granted either only by the US or European patent office. Many obviously do not know that there is no license required. Most of the CGIAR centers are based in developing countries which have not granted those patents so far and they serve client countries which do not usually grant those patents. So the actual freedom to operate is not that much affected. (M9/729-40)	71. [Industry$_2$] There is a need to educate people as to the legal nature of intellectual property: no extra-territorial influence, research exemptions, national emergency provisions, compulsory licenses. (M9/827)
	72. Information is also needed on whether research institutions, concerned about their relations with donors, are avoiding technologies that they are legally free to use in a limited context. Will international agricultural research institutes, for example, distribute crop varieties containing a Bt gene that is unpatented in developing countries, but patented in donor countries? (Straus, 2001)	
Infringements not sued against poor farmers?	74. [NGO$_3$] [This is hardly general practice.] There are hundreds of prosecutions of farmers in North America over the question of the drifting of pollen from field to field. (M9/385-9)	73. [Industry$_2$] People who will be saving seed and planting materials and using it themselves are … not examples of infringement that cause us any concern; we don't pursue anonymous infringement, we can't afford it, we're not rich enough (M9/309-12)

Issues	Pro	Contra
Invalid patents	75. [Industry$_2$] [There are examples] The Mexican white bean variety that was taken from Mexico somewhere and patented; it was derived and so most patent laws of the world would say that that's not patentable. (M9/952-5)	
Legal remedies too expensive?	77. [NGO$_8$] Sometimes people are actually intimidated by the existence of the patent and do not spend millions of dollars litigating. (M9/305-6)	76. [Industry$_2$] Litigation on a patent is extremely expensive. It is not reasonable to assume that [Company] would assert a patent against an entity in Mexico knowing it was invalid. We do not operate that way. (M9/299-302)
		78. [Industry$_3$] Since there are so few patents granted to companies from the North in poor Southern countries the problem is not relevant. (M9/657-61)
Capacity to litigate patents	79. [NGO$_8$] Bristol-Myers got through the patent office in Thailand a formulation patent that was in fact rejected in the US as not being novel. It's a famous case within the access to medicine of a bogus patent. … To give people in the south recourse to the western size court system doesn't really mean the same right. (M9/666-693)	
	80. [NGO$_8$] A poor country cannot really litigate patents, they do not have the capacity to undo a bad claim. (M9/649-54)	
Easier mechanism to revoke patents?	82. [Expert$_2$] Given that many of the developing countries accept patent presentations on the basis that they have been granted in the US or in Europe… there could be a simplified procedure to revoke patents in developing countries which have been revoked in the northern country. I think that is at least an idea maybe one could agree on. (M9/709-16)	81. [Industry$_2$] When companies litigate in the United States they seek access to the file wrapper of the European Patent Office, and conversely … to look for arguments to determine whether patentability was correct. That's routinely done around the world at present. (M9/720-3)
Barriers to Technology Transfer?	83. IPRs have an impact on the objectives of the Convention on Biological Diversity, this is most likely to occur in the context of technology transfer, rather than in the context of conservation and sustainable use. … Parties will need to take steps cooperatively to manage the influence of IPR to ensure that it is positive rather than negative. (UNEP/CBD/COP/3/22, paragraph 5)	84. Rules exist that require the contracting parties to the CBD to make technology using germplasm available to the provider countries on mutually agreed terms. This applies explicitly to technology protected by patents and other intellectual property rights … and includes transfer to private companies in the developing countries. (Seiler, Dutfield, 2001)

Issues	Pro	Contra
		85. One of the key arguments made by advocates of stronger global IPRs is that such a system, as embodied in the TRIPS Agreement, would increase Foreign Direct Investment (FDI) in, and associated technology transfers to, developing countries. Theoretical analysis suggests that the impact of protecting IPRs is likely to be positive, although relatively unimportant in relation to other determinants of FDI. (UNCTAD, 1996)
	86. The transfer of technology is important in enabling sustainable development. Both TRIPS (Art. 7) and the CBD seek to foster the transfer of technology. Art. 7 of TRIPS refers to the "transfer and dissemination of technology, to the mutual advantage of producers and users of technological knowledge". Importantly Article 40.1 of TRIPS recognizes that the licensing or other use of intellectual property rights "may impede the transfer and dissemination of technology". (EU/CEAS, 2000)	87. The objectives of promoting technological innovation and the transfer of technology are usually mutually consistent since right holders are generally more willing to transfer technology voluntarily where a country's IPR system provides effective protection. In addition, the disclosure requirements of the patent system and exceptions to patent rights for experimental use are designed to maximize the degree to which knowledge of new technology becomes publicly available and can be the basis for further technological development. (WTO-CTE, 1995)
Cooperation		88. [Industry$_2$] [For us] it's much more profitable and interesting to be cooperative and to collaborate with people who are looking for research access to key-enabling technologies. (M9/314-20)
		89. [Industry$_1$] [In joint ventures with developing countries] we are only concerned that the rights we contribute will be used in that country and that the product that results will be used within that country and there is no export that would undercut other prior obligations. To that extent it really doesn't matter to us whether intellectual property rights were created. (M9/337-45)
Freedom to operate of DC partners	90. [Industry$_2$] [In case the company excludes the right to export products resulting from the research cooperation] this may affect the viability of the product developed in the DC for the local entity. For example, economies of scale may not be achieved. In the worst case [such control] can [annul] the creativity and inventiveness of the local arena. (M9/542-5)	

Questions posed to the participants

- Patents restrict, by definition, free access to protected technologies. Do DCs face specific problems in this respect if (and because) patent protection is extended to genes? What is the difference if technologies implying chemical compounds are patented?
- Is there a need for mechanisms that make it easier for DCs to revoke patents that have already been challenged (invalidated) in Northern countries?
- What can be done to make the cooperative strategies of companies (patent holders) reliable and stable?
- Should (and could) patent laws be accommodated in the DCs to support and assure such cooperation?

E2 Points to be Considered for Conclusions

- Patents restrict, by definition, free access to protected technologies. Do DCs face specific problems in this respect if (and because) patent protection is extended to genes? What is the difference if technologies implying chemical compounds are patented?
- Is there a need for mechanisms that make it easier for DCs to revoke patents that have already been challenged (invalidated) in Northern countries?
- What can be done to make the cooperative strategies of companies (patent holders) reliable and stable?
- Should (and could) patent laws be accommodated in the DCs to support and assure such cooperation?

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